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(54) Title: OLIGONUCLEOTIDE MEDIATED INHIBITION OF HEPATITIS B VIRUS AND HEPATITIS C VIRUS REPLICATION

(57) Abstract: The present invention relates to nucleic acid molecules, including antisense and enzymatic nucleic acid molecules, such as hammerhead ribozymes, DNAzymes, Inozymes, Zinzymes, Amberzymes, and G-cleaver ribozymes, which modulate the synthesis, expression and/or stability of an HCV or HBV RNA and methods for their use alone or in combination with other therapies. In addition, nucleic acid decoy molecules and aptamers that bind to HBV reverse transcriptase and/or HBV reverse transcriptase primer sequences and methods for their use alone or in combination with other therapies, are disclosed. Oligonucleotides that specifically bind the Enhancer I region of HBV DNA are further disclosed. The present invention further relates to the use of nucleic acids, such as decoy and aptamer molecules of the invention, to modulate the expression of Hepatitis B virus (HBV) genes and HBV viral replication. Furthermore, HBV animal models and methods of use are disclosed, including methods of screening for compounds and/or potential therapies directed against HBV. The present invention also relates to compounds, including enzymatic nucleic acid molecules, ribozymes, DNAzymes, nuclease activating compounds and chimeras such as 2',5'-adenylates, that modulate the expression and/or replication of hepatitis C virus (HCV).



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DESCRIPTION

OLIGONUCLEOTIDE MEDIATED INHIBITION OF HEPATITIS B VIRUS AND HEPATITIS C VIRUS REPLICATION

Background Of The Invention

This patent application claims priority from Blatt et al., USSN (09/817,879), filed March 26, 2001, which is a continuation-in-part of Blatt et al., USSN (09/740,332), filed December 18, 2000, which is a continuation-in-part of Blatt et al., USSN (09/611,931), filed July 7, 2000, which is a continuation-in-part of Blatt et al., 09/504,321, filed February 15, 2000, which is a continuation-in-part of Blatt et al., USSN 09/274,553, filed March 23, 1999, which is a continuation-in-part of Blatt et al., USSN 09/257,608, filed February 24, 1999 (abandoned), which claims priority from Blatt et al., USSN 60/100,842, filed September 18, 1998, and McSwiggen et al., USSN 60/083,217 filed April 27, 1998; all of these earlier applications are entitled "ENZYMATIC NUCLEIC ACID TREATMENT OF DISEASES OR CONDITIONS RELATED TO HEPATITIS C VIRUS INFECTION". This patent application also claims priority from Draper et al., USSN 09/877,478 filed June 8, 2001, which is a continuation-in-part of Draper et al., USSN (09/696,347), filed October 24, 2000, which is a continuation-in-part of Draper et al., USSN (09/636,385), filed August 9, 2000, which is a continuation in part of Draper et al., USSN (09/531,025), filed March 20, 2000, which is a continuation in part of Draper, USSN (09/436,430), filed November 8, 1999, which is a continuation of USSN (08/193,627), filed February 7, 1994, now US patent No. 6,017,756, which is a continuation of USSN (07/882,712), filed May 14, 1992, now abandoned; all of these earlier applications are entitled "METHOD AND REAGENT FOR INHIBITING HEPATITIS B VIRUS REPLICATION". This patent application also claims priority from Macejak et al., USSN (60/335,059), filed October 24, 2001, Macejak et al., USSN (60/296,876), filed June 8, 2001, and Morrissey et al., USSN (60/337,055), filed December 5, 2001. These applications are hereby incorporated by reference herein in their entireties, including the drawings.

The present invention concerns compounds, compositions, and methods for the study, diagnosis, and treatment of degenerative and disease states related to hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, replication and gene expression. Specifically, the invention relates to nucleic acid molecules used to modulate expression of HBV and HCV. In

addition, the instant invention relates to methods, models and systems for screening inhibitors of HBV and HCV replication and propagation.

The following is a discussion of relevant art pertaining to hepatitis B virus (HBV) and hepatitis C virus (HCV). The discussion is not meant to be complete and is provided only for understanding of the invention that follows. The summary is not an admission that any of the work described below is prior art to the claimed invention.

In 1989, the Hepatitis C Virus (HCV) was determined to be an RNA virus and was identified as the causative agent of most non-A non-B viral Hepatitis (Choo *et al.*, *Science*. 1989; 244:359-362). Unlike retroviruses such as HIV, HCV does not go through a DNA replication phase and no integrated forms of the viral genome into the host chromosome have been detected (Houghton *et al.*, *Hepatology* 1991;14:381-388). Rather, replication of the coding (plus) strand is mediated by the production of a replicative (minus) strand leading to the generation of several copies of plus strand HCV RNA. The genome consists of a single, large, open-reading frame that is translated into a polyprotein (Kato *et al.*, *FEBS Letters*. 1991; 280: 325-328). This polyprotein subsequently undergoes post-translational cleavage, producing several viral proteins (Leinbach *et al.*, *Virology*. 1994: 204:163-169).

Examination of the 9.5-kilobase genome of HCV has demonstrated that the viral nucleic acid can mutate at a high rate (Smith *et al.*, *Mol. Evol.* 1997 45:238-246). This rate of mutation has led to the evolution of several distinct genotypes of HCV that share approximately 70% sequence identity (Simmonds *et al.*, *J. Gen. Virol.* 1994;75 :1053-1061). It is important to note that these sequences are evolutionarily quite distant. For example, the genetic identity between humans and primates such as the chimpanzee is approximately 98%. In addition, it has been demonstrated that an HCV infection in an individual patient is composed of several distinct and evolving quasispecies that have 98% identity at the RNA level. Thus, the HCV genome is hypervariable and continuously changing. Although the HCV genome is hypervariable, there are 3 regions of the genome that are highly conserved. These conserved sequences occur in the 5' and 3' non-coding regions as well as the 5'-end of the core protein coding region and are thought to be vital for HCV RNA replication as well as translation of the HCV polyprotein. Thus, therapeutic agents that target these conserved HCV genomic regions can have a significant impact over a wide range of HCV genotypes. Moreover, it is unlikely that drug resistance will occur with enzymatic nucleic acids specific to conserved regions of the HCV genome. In contrast, therapeutic modalities that target inhibition of enzymes such as the viral proteases or helicase are likely to result in the selection for drug resistant strains since the RNA for these viral encoded enzymes is located in the hypervariable portion of the HCV genome.

After initial exposure to HCV, the patient experiences a transient rise in liver enzymes, which indicates the occurrence of inflammatory processes (Alter *et al.*, *IN*: Seeff LB, Lewis JH, eds. *Current Perspectives in Hepatology*. New York: Plenum Medical Book Co; 1989:83-89). This elevation in liver enzymes will occur at least 4 weeks after the initial exposure and can last for up to two months (Farci *et al.*, *New England Journal of Medicine*. 1991;325:98-104). Prior to the rise in liver enzymes, it is possible to detect HCV RNA in the patient's serum using RT-PCR analysis (Takahashi *et al.*, *American Journal of Gastroenterology*. 1993;88:2:240-243). This stage of the disease is called the acute stage and usually goes undetected since 75% of patients with acute viral hepatitis from HCV infection are asymptomatic. The remaining 25% of these patients develop jaundice or other symptoms of hepatitis.

Acute HCV infection is a benign disease, however, and as many as 80% of acute HCV patients progress to chronic liver disease as evidenced by persistent elevation of serum alanine aminotransferase (ALT) levels and by continual presence of circulating HCV RNA (Sherlock, *Lancet* 1992; 339:802). The natural progression of chronic HCV infection over a 10 to 20 year period leads to cirrhosis in 20 to 50% of patients (Davis *et al.*, *Infectious Agents and Disease* 1993;2:150:154) and progression of HCV infection to hepatocellular carcinoma has been well documented (Liang *et al.*, *Hepatology*. 1993; 18:1326-1333; Tong *et al.*, *Western Journal of Medicine*, 1994; Vol. 160, No. 2: 133-138). There have been no studies that have determined sub-populations that are most likely to progress to cirrhosis and/or hepatocellular carcinoma, thus all patients have equal risk of progression.

It is important to note that the survival for patients diagnosed with hepatocellular carcinoma is only 0.9 to 12.8 months from initial diagnosis (Takahashi *et al.*, *American Journal of Gastroenterology*. 1993;88:2:240-243). Treatment of hepatocellular carcinoma with chemotherapeutic agents has not proven effective and only 10% of patients will benefit from surgery due to extensive tumor invasion of the liver (Trinchet *et al.*, *Presse Medicin*. 1994;23:831-833). Given the aggressive nature of primary hepatocellular carcinoma, the only viable treatment alternative to surgery is liver transplantation (Pichlmayr *et al.*, *Hepatology*. 1994;20:33S-40S).

Upon progression to cirrhosis, patients with chronic HCV infection present with clinical features, which are common to clinical cirrhosis regardless of the initial cause (D'Amico *et al.*, *Digestive Diseases and Sciences*. 1986;31:5: 468-475). These clinical features can include: bleeding esophageal varices, ascites, jaundice, and encephalopathy (Zakim D, Boyer TD. *Hepatology a textbook of liver disease*. Second Edition Volume 1. 1990 W.B. Saunders Company. Philadelphia). In the early stages of cirrhosis, patients are classified as compensated, meaning that although liver tissue damage has occurred, the patient's liver is still able to detoxify metabolites in the blood-stream. In addition, most

patients with compensated liver disease are asymptomatic and the minority with symptoms report only minor symptoms such as dyspepsia and weakness. In the later stages of cirrhosis, patients are classified as decompensated meaning that their ability to detoxify metabolites in the bloodstream is diminished and it is at this stage that the clinical features described above will present.

In 1986, D'Amico *et al.* described the clinical manifestations and survival rates in 1155 patients with both alcoholic and viral associated cirrhosis (D'Amico *supra*). Of the 1155 patients, 435 (37%) had compensated disease although 70% were asymptomatic at the beginning of the study. The remaining 720 patients (63%) had decompensated liver disease with 78% presenting with a history of ascites, 31% with jaundice, 17% had bleeding and 16% had encephalopathy. Hepatocellular carcinoma was observed in six (.5%) patients with compensated disease and in 30 (2.6%) patients with decompensated disease.

Over the course of six years, the patients with compensated cirrhosis developed clinical features of decompensated disease at a rate of 10% per year. In most cases, ascites was the first presentation of decompensation. In addition, hepatocellular carcinoma developed in 59 patients who initially presented with compensated disease by the end of the six-year study.

With respect to survival, the D'Amico study indicated that the five-year survival rate for all patients on the study was only 40%. The six-year survival rate for the patients who initially had compensated cirrhosis was 54%, while the six-year survival rate for patients who initially presented with decompensated disease was only 21%. There were no significant differences in the survival rates between the patients who had alcoholic cirrhosis and the patients with viral related cirrhosis. The major causes of death for the patients in the D'Amico study were liver failure in 49%; hepatocellular carcinoma in 22%; and, bleeding in 13% (D'Amico *supra*).

Chronic Hepatitis C is a slowly progressing inflammatory disease of the liver, mediated by a virus (HCV) that can lead to cirrhosis, liver failure and/or hepatocellular carcinoma over a period of 10 to 20 years. In the US, it is estimated that infection with HCV accounts for 50,000 new cases of acute hepatitis in the United States each year (NIH Consensus Development Conference Statement on Management of Hepatitis C March 1997). The prevalence of HCV in the United States is estimated at 1.8% and the CDC places the number of chronically infected Americans at approximately 4.5 million people. The CDC also estimates that up to 10,000 deaths per year are caused by chronic HCV infection. The prevalence of HCV in the United States is estimated at 1.8% and the CDC places the number of chronically infected Americans at approximately 4.5 million people. The CDC also estimates that up to 10,000 deaths per year are caused by chronic HCV infection.

Numerous well controlled clinical trials using interferon (IFN-alpha) in the treatment of chronic HCV infection have demonstrated that treatment three times a week results in lowering of serum ALT values in approximately 50% (range 40% to 70%) of patients by the end of 6 months of therapy (Davis *et al.*, *New England Journal of Medicine* 1989; 321:1501-1506; Marcellin *et al.*, *Hepatology*. 1991; 13:393-397; Tong *et al.*, *Hepatology* 1997;26:747-754; Tong *et al.*, *Hepatology* 1997 26(6): 1640-1645). However, following cessation of interferon treatment, approximately 50% of the responding patients relapsed, resulting in a "durable" response rate as assessed by normalization of serum ALT concentrations of approximately 20 to 25%.

In recent years, direct measurement of the HCV RNA has become possible through use of either the branched-DNA or Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) analysis. In general, the RT-PCR methodology is more sensitive and leads to more accurate assessment of the clinical course (Tong *et al.*, *supra*). Studies that have examined six months of type 1 interferon therapy using changes in HCV RNA values as a clinical endpoint have demonstrated that up to 35% of patients will have a loss of HCV RNA by the end of therapy (Marcellin *et al.*, *supra*). However, as with the ALT endpoint, about 50% of the patients relapse six months following cessation of therapy resulting in a durable virologic response of only 12% (Marcellin *et al.*, *supra*). Studies that have examined 48 weeks of therapy have demonstrated that the sustained virological response is up to 25% (NIH consensus statement: 1997). Thus, standard of care for treatment of chronic HCV infection with type 1 interferon is now 48 weeks of therapy using changes in HCV RNA concentrations as the primary assessment of efficacy (Hoofnagle *et al.*, *New England Journal of Medicine* 1997; 336(5) 347-356).

Side effects resulting from treatment with type 1 interferons can be divided into four general categories, which include 1. Influenza-like symptoms; 2. Neuropsychiatric; 3. Laboratory abnormalities; and, 4. Miscellaneous (Dusheiko *et al.*, *Journal of Viral Hepatitis*. 1994;1:3-5). Examples of influenza-like symptoms include; fatigue, fever; myalgia; malaise; appetite loss; tachycardia; rigors; headache and arthralgias. The influenza-like symptoms are usually short-lived and tend to abate after the first four weeks of dosing (Dushieko *et al.*, *supra*). Neuropsychiatric side effects include: irritability, apathy; mood changes; insomnia; cognitive changes and depression. The most important of these neuropsychiatric side effects is depression and patients who have a history of depression should not be given type 1 interferon. Laboratory abnormalities include; reduction in myeloid cells including granulocytes, platelets and to a lesser extent red blood cells. These changes in blood cell counts rarely lead to any significant clinical sequelae (Dushieko *et al.*, *supra*). In addition, increases in triglyceride concentrations and elevations in serum alanine and aspartate aminotransferase concentration have been observed. Finally, thyroid abnormalities have been reported. These thyroid abnormalities are usually reversible after cessation of interferon

therapy and can be controlled with appropriate medication while on therapy. Miscellaneous side effects include nausea; diarrhea; abdominal and back pain; pruritus; alopecia; and rhinorrhea. In general, most side effects will abate after 4 to 8 weeks of therapy (Dushieko *et al.*, *supra*).

Type 1 Interferon is a key constituent of many treatment programs for chronic HCV infection. Treatment with type 1 interferon induces a number of genes and results in an antiviral state within the cell. One of the genes induced is 2', 5' oligoadenylate synthetase, an enzyme that synthesizes short 2', 5' oligoadenylate (2-5A) molecules. Nascent 2-5A subsequently activates a latent RNase, RNase L, which in turn nonspecifically degrades viral RNA.

Chronic hepatitis B is caused by an enveloped virus, commonly known as the hepatitis B virus or HBV. HBV is transmitted via infected blood or other body fluids, especially saliva and semen, during delivery, sexual activity, or sharing of needles contaminated by infected blood. Individuals may be "carriers" and transmit the infection to others without ever having experienced symptoms of the disease. Persons at highest risk are those with multiple sex partners, those with a history of sexually transmitted diseases, parenteral drug users, infants born to infected mothers, "close" contacts or sexual partners of infected persons, and healthcare personnel or other service employees who have contact with blood. Transmission is also possible via tattooing, ear or body piercing, and acupuncture; the virus is also stable on razors, toothbrushes, baby bottles, eating utensils, and some hospital equipment such as respirators, scopes and instruments. There is no evidence that HBsAg positive food handlers pose a health risk in an occupational setting, nor should they be excluded from work. Hepatitis B has never been documented as being a food-borne disease. The average incubation period is 60 to 90 days, with a range of 45 to 180; the number of days appears to be related to the amount of virus to which the person was exposed. However, determining the length of incubation is difficult, since onset of symptoms is insidious. Approximately 50% of patients develop symptoms of acute hepatitis that last from 1 to 4 weeks. Two percent or less of these individuals develop fulminant hepatitis resulting in liver failure and death.

The determinants of severity include: (1) The size of the dose to which the person was exposed; (2) the person's age with younger patients experiencing a milder form of the disease; (3) the status of the immune system with those who are immunosuppressed experiencing milder cases; and (4) the presence or absence of co-infection with the Delta virus (hepatitis D), with more severe cases resulting from co-infection. In symptomatic cases, clinical signs include loss of appetite, nausea, vomiting, abdominal pain in the right upper quadrant, arthralgia, and tiredness/loss of energy. Jaundice is not experienced in all

cases, however, jaundice is more likely to occur if the infection is due to transfusion or percutaneous serum transfer, and it is accompanied by mild pruritus in some patients. Bilirubin elevations are demonstrated in dark urine and clay-colored stools, and liver enlargement may occur accompanied by right upper-quadrant pain. The acute phase of the disease may be accompanied by severe depression, meningitis, Guillain-Barré syndrome, myelitis, encephalitis, agranulocytosis, and/or thrombocytopenia.

Hepatitis B is generally self-limiting and will resolve in approximately 6 months. Asymptomatic cases can be detected by serologic testing, since the presence of the virus leads to production of large amounts of HBsAg in the blood. This antigen is the first and most useful diagnostic marker for active infections. However, if HBsAg remains positive for 20 weeks or longer, the person is likely to remain positive indefinitely and is now a carrier. While only 10% of persons over age 6 who contract HBV become carriers, 90% of infants infected during the first year of life do so.

Hepatitis B virus (HBV) infects over 300 million people worldwide (Imperial, 1999, *Gastroenterol. Hepatol.*, 14 (suppl), S1-5). In the United States, approximately 1.25 million individuals are chronic carriers of HBV as evidenced by the fact that they have measurable hepatitis B virus surface antigen HBsAg in their blood. The risk of becoming a chronic HBsAg carrier is dependent upon the mode of acquisition of infection as well as the age of the individual at the time of infection. For those individuals with high levels of viral replication, chronic active hepatitis with progression to cirrhosis, liver failure and hepatocellular carcinoma (HCC) is common, and liver transplantation is the only treatment option for patients with end-stage liver disease from HBV.

The natural progression of chronic HBV infection over a 10 to 20 year period leads to cirrhosis in 20-to-50% of patients and progression of HBV infection to hepatocellular carcinoma has been well documented. There have been no studies that have determined sub-populations that are most likely to progress to cirrhosis and/or hepatocellular carcinoma, thus all patients have equal risk of progression.

It is important to note that the survival for patients diagnosed with hepatocellular carcinoma is only 0.9 to 12.8 months from initial diagnosis (Takahashi *et al.*, 1993, *American Journal of Gastroenterology*, 88, 240-243). Treatment of hepatocellular carcinoma with chemotherapeutic agents has not proven effective and only 10% of patients will benefit from surgery due to extensive tumor invasion of the liver (Trinchet *et al.*, 1994, *Presse Medicine*, 23, 831-833). Given the aggressive nature of primary hepatocellular carcinoma, the only viable treatment alternative to surgery is liver transplantation (Pichlmayr *et al.*, 1994, *Hepatology*, 20, 33S-40S).

Upon progression to cirrhosis, patients with chronic HCV and HBV infection present with clinical features, which are common to clinical cirrhosis regardless of the initial cause (D'Amico *et al.*, 1986, *Digestive Diseases and Sciences*, 31, 468-475). These clinical features may include: bleeding esophageal varices, ascites, jaundice, and encephalopathy (Zakim D, Boyer TD. *Hepatology a textbook of liver disease*, Second Edition Volume 1. 1990 W.B. Saunders Company. Philadelphia). In the early stages of cirrhosis, patients are classified as compensated, meaning that although liver tissue damage has occurred, the patient's liver is still able to detoxify metabolites in the blood-stream. In addition, most patients with compensated liver disease are asymptomatic and the minority with symptoms report only minor symptoms such as dyspepsia and weakness. In the later stages of cirrhosis, patients are classified as decompensated meaning that their ability to detoxify metabolites in the bloodstream is diminished and it is at this stage that the clinical features described above will present.

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Hepatitis B virus is a double-stranded circular DNA virus. It is a member of the Hepadnaviridae family. The virus consists of a central core that contains a core antigen (HBcAg) surrounded by an envelope containing a surface protein/surface antigen (HBsAg)

and is 42 nm in diameter. It also contains an e antigen (HBeAg), which, along with HBcAg and HBsAg, is helpful in identifying this disease.

In HBV virions, the genome is found in an incomplete double-stranded form. HBV uses a reverse transcriptase to transcribe a positive-sense full length RNA version of its genome back into DNA. This reverse transcriptase also contains DNA polymerase activity and thus begins replicating the newly synthesized minus-sense DNA strand. However, it appears that the core protein encapsidates the reverse-transcriptase/polymerase before it completes replication.

From the free-floating form, the virus must first attach itself specifically to a host cell membrane. Viral attachment is one of the crucial steps that determines host and tissue specificity. However, currently there are no *in vitro* cell-lines that can be infected by HBV. There are some cells lines, such as HepG2, which can support viral replication only upon transient or stable transfection using HBV DNA.

After attachment, fusion of the viral envelope and host membrane must occur to allow the viral core proteins containing the genome and polymerase to enter the cell. Once inside, the genome is translocated to the nucleus where it is repaired and cyclized.

The complete closed circular DNA genome of HBV remains in the nucleus and gives rise to four transcripts. These transcripts initiate at unique sites but share the same 3'-ends. The 3.5-kb pregenomic RNA serves as a template for reverse transcription and also encodes the nucleocapsid protein and polymerase. A subclass of this transcript with a 5'-end extension codes for the precore protein that, after processing, is secreted as HBV e antigen. The 2.4-kb RNA encompasses the pre-S1 open reading frame (ORF) that encodes the large surface protein. The 2.1-kb RNA encompasses the pre-S2 and S ORFs that encode the middle and small surface proteins, respectively. The smallest transcript (~0.8-kb) codes for the X protein, a transcriptional activator.

Multiplication of the HBV genome begins within the nucleus of an infected cell. RNA polymerase II transcribes the circular HBV DNA into greater-than-full length mRNA. Since the mRNA is longer than the actual complete circular DNA, redundant ends are formed. Once produced, the pregenomic RNA exits the nucleus and enters the cytoplasm.

The packaging of pregenomic RNA into core particles is triggered by the binding of the HBV polymerase to the 5' epsilon stem-loop. RNA encapsidation is believed to occur as soon as binding occurs. The HBV polymerase also appears to require associated core protein in order to function. The HBV polymerase initiates reverse transcription from the 5' epsilon stem-loop three to four base pairs at which point the polymerase and attached nascent DNA

are transferred to the 3' copy of the DR1 region. Once there, the (-)DNA is extended by the HBV polymerase while the RNA template is degraded by the HBV polymerase RNase H activity. When the HBV polymerase reaches the 5' end, a small stretch of RNA is left undigested by the RNase H activity. This segment of RNA is comprised of a small sequence just upstream and including the DR1 region. The RNA oligomer is then translocated and annealed to the DR2 region at the 5' end of the (-)DNA. It is used as a primer for the (+)DNA synthesis which is also generated by the HBV polymerase. It appears that the reverse transcription as well as plus strand synthesis may occur in the completed core particle.

Since the pregenomic RNA is required as a template for DNA synthesis, this RNA is an excellent target for nucleic acid based therapeutics. Nucleoside analogues that have been documented to modulate HBV replication target the reverse transcriptase activity needed to convert the pregenomic RNA into DNA. Nucleic acid decoy and aptamer modulation of HBV reverse transcriptase would be expected to result in a similar modulation of HBV replication.

Current therapeutic goals of treatment are three-fold: to eliminate infectivity and transmission of HBV to others, to arrest the progression of liver disease and improve the clinical prognosis, and to prevent the development of hepatocellular carcinoma (HCC).

Interferon alpha use is the most common therapy for HBV; however, recently Lamivudine (3TC®) has been approved by the FDA. Interferon alpha (IFN-alpha) is one treatment for chronic hepatitis B. The standard duration of IFN-alpha therapy is 16 weeks, however, the optimal treatment length is still poorly defined. A complete response (HBV DNA negative HBeAg negative) occurs in approximately 25% of patients. Several factors have been identified that predict a favorable response to therapy including: High ALT, low HBV DNA, being female, and heterosexual orientation.

There is also a risk of reactivation of the hepatitis B virus even after a successful response, this occurs in around 5% of responders and normally occurs within 1 year.

Side effects resulting from treatment with type 1 interferons can be divided into four general categories including: Influenza-like symptoms, neuropsychiatric, laboratory abnormalities, and other miscellaneous side effects. Examples of influenza-like symptoms include, fatigue, fever, myalgia, malaise, appetite loss, tachycardia, rigors, headache and arthralgias. The influenza-like symptoms are usually short-lived and tend to abate after the first four weeks of dosing (Dusheiko *et al.*, 1994, *Journal of Viral Hepatitis*, 1, 3-5). Neuropsychiatric side effects include irritability, apathy, mood changes, insomnia, cognitive

changes, and depression. Laboratory abnormalities include the reduction of myeloid cells, including granulocytes, platelets and to a lesser extent, red blood cells. These changes in blood cell counts rarely lead to any significant clinical sequelae. In addition, increases in triglyceride concentrations and elevations in serum alanine and aspartate aminotransferase concentration have been observed. Finally, thyroid abnormalities have been reported. These thyroid abnormalities are usually reversible after cessation of interferon therapy and can be controlled with appropriate medication while on therapy. Miscellaneous side effects include nausea, diarrhea, abdominal and back pain, pruritus, alopecia, and rhinorrhea. In general, most side effects will abate after 4 to 8 weeks of therapy (Dushieko *et al.*, *supra*).

Lamivudine (3TC®) is a nucleoside analogue, which is a very potent and specific inhibitor of HBV DNA synthesis. Lamivudine has recently been approved for the treatment of chronic Hepatitis B. Unlike treatment with interferon, treatment with 3TC® does not eliminate the HBV from the patient. Rather, viral replication is controlled and chronic administration results in improvements in liver histology in over 50% of patients. Phase III studies with 3TC®, showed that treatment for one year was associated with reduced liver inflammation and a delay in scarring of the liver. In addition, patients treated with Lamivudine (100mg per day) had a 98 percent reduction in hepatitis B DNA and a significantly higher rate of seroconversion, suggesting disease improvements after completion of therapy. However, stopping of therapy resulted in a reactivation of HBV replication in most patients. In addition recent reports have documented 3TC® resistance in approximately 30% of patients.

Current therapies for treating HBV infection, including interferon and nucleoside analogues, are only partially effective. In addition, drug resistance to nucleoside analogues is now emerging, making treatment of chronic Hepatitis B more difficult. Thus, a need exists for effective treatment of this disease that utilizes antiviral modulators that work by mechanisms other than those currently utilized in the treatment of both acute and chronic hepatitis B infections.

Welch *et al.*, *Gene Therapy* 1996 3(11): 994-1001 describe *in vitro* and *in vivo* studies with two vector expressed hairpin ribozymes targeted against hepatitis C virus.

Sakamoto *et al.*, *J. Clinical Investigation* 1996 98(12): 2720-2728 describe intracellular cleavage of hepatitis C virus RNA and inhibition of viral protein translation by certain vector expressed hammerhead ribozymes.

Lieber *et al.*, *J. Virology* 1996 70(12): 8782-8791 describe elimination of hepatitis C virus RNA in infected human hepatocytes by adenovirus-mediated expression of certain hammerhead ribozymes.

Ohkawa *et al.*, 1997, *J. Hepatology*, 27; 78-84, describe *in vitro* cleavage of HCV RNA and inhibition of viral protein translation using certain *in vitro* transcribed hammerhead ribozymes.

Barber *et al.*, International PCT Publication No. *WO 97/32018*, describe the use of an adenovirus vector to express certain anti-hepatitis C virus hairpin ribozymes.

Kay *et al.*, International PCT Publication No. *WO 96/18419*, describe certain recombinant adenovirus vectors to express anti-HCV hammerhead ribozymes.

Yamada *et al.*, Japanese Patent Application No. *JP 07231784* describe a specific poly-(L)-lysine conjugated hammerhead ribozyme targeted against HCV.

Draper, U.S. Patent Nos. 5,610,054 and 5,869,253, describes enzymatic nucleic acid molecules capable of inhibiting replication of HCV.

Macejak. *et al.*, 2000, *Hepatology*, 31, 769-776, describe enzymatic nucleic acid molecules capable of inhibiting replication of HCV.

Weifeng and Torrence, 1997, *Nucleosides and Nucleotides*, 16, 7-9, describe the synthesis of 2-5A antisense chimeras with various non-nucleoside components.

Torrence *et al.*, US patent No. 5,583,032 describe targeted cleavage of RNA using an antisense oligonucleotide linked to a 2',5'-oligoadenylate activator of RNase L.

Suhadolnik and Pfeleiderer, US patent Nos. 5,863,905; 5,700,785; 5,643,889; 5,556,840; 5,550,111; 5,405,939; 5,188,897; 4,924,624; and 4,859,768 describe specific internucleotide phosphorothioate 2',5'-oligoadenylates and 2',5'-oligoadenylate conjugates.

Budowsky *et al.*, US patent No. 5,962,431 describe a method of treating papillomavirus using specific 2',5'-oligoadenylates.

Torrence *et al.*, International PCT publication No. *WO 00/14219*, describe specific peptide nucleic acid 2',5'-oligoadenylate chimeric molecules.

Stinchcomb *et al.*, US patent No. 5,817,796, describe C-myb ribozymes having 2'-5'-Linked Adenylate Residues.

Draper, US patent No. 6,017,756, describes the use of ribozymes for the inhibition of Hepatitis B Virus.

Passman *et al.*, 2000, *Biochem. Biophys. Res. Commun.*, 268(3), 728-733.; Gan *et al.*, 1998, *J. Med. Coll. PLA*, 13(3), 157-159.; Li *et al.*, 1999, *Jiefangjun Yixue Zazhi*, 24(2), 99-

101.; Putlitz *et al.*, 1999, *J. Virol.*, 73(7), 5381-5387.; Kim *et al.*, 1999, *Biochem. Biophys. Res. Commun.*, 257(3), 759-765.; Xu *et al.*, 1998, *Bingdu Xuebao*, 14(4), 365-369.; Welch *et al.*, 1997, *Gene Ther.*, 4(7), 736-743.; Goldenberg *et al.*, 1997, International PCT publication No. WO 97/08309, Wands *et al.*, 1997, *J. of Gastroenterology and Hepatology*, 12(suppl.), S354-S369.; Ruiz *et al.*, 1997, *BioTechniques*, 22(2), 338-345.; Gan *et al.*, 1996, *J. Med. Coll. PLA*, 11(3), 171-175.; Beck and Nassal, 1995, *Nucleic Acids Res.*, 23(24), 4954-62.; Goldenberg, 1995, International PCT publication No. WO 95/22600.; Xu *et al.*, 1993, *Bingdu Xuebao*, 9(4), 331-6.; Wang *et al.*, 1993, *Bingdu Xuebao*, 9(3), 278-80, all describe ribozymes that are targeted to cleave a specific HBV target site.

Hunt *et al.*, US patent No. 5,859,226, describes specific non-naturally occurring oligonucleotide decoys intended to inhibit the expression of MHC-II genes through binding of the RF-X transcription factor, that can inhibit the expression of certain HBV and CMV viral proteins.

Kao *et al.*, International PCT Publication No. WO 00/04141, describes linear single stranded nucleic acid molecules capable of specifically binding to viral polymerases and inhibiting the activity of the viral polymerase.

Lu, International PCT Publication No. WO 99/20641, describes specific triplex-forming oligonucleotides used in treating HBV infection.

SUMMARY OF THE INVENTION

This invention relates to enzymatic nucleic acid molecules that can disrupt the function of RNA species of hepatitis B virus (HBV), hepatitis C virus (HCV) and/or those RNA species encoded by HBV or HCV. In particular, applicant provides enzymatic nucleic acid molecules capable of specifically cleaving HBV RNA or HCV RNA and describes the selection and function thereof. Such enzymatic nucleic acid molecules can be used to treat diseases and disorders associated with HBV and HCV infection.

In one embodiment, the invention features an enzymatic nucleic acid molecule that specifically cleaves RNA derived from hepatitis B virus (HBV), wherein the enzymatic nucleic acid molecule comprises sequence defined as Seq. ID No. 10887.

In another embodiment, the invention features a composition comprising an enzymatic nucleic acid molecule of the invention and a pharmaceutically acceptable carrier.

In another embodiment, the invention features a mammalian cell, for example a human cell, comprising an enzymatic nucleic acid molecule contemplated by the invention.

In one embodiment, the invention features a method for the treatment of cirrhosis, liver failure or hepatocellular carcinoma comprising administering to a patient an enzymatic nucleic acid molecule of the invention under conditions suitable for the treatment.

In another embodiment, the invention features a method for the treatment of a patient having a condition associated with HBV and/or HCV infection, comprising contacting cells of said patient with an enzymatic nucleic acid molecule of the invention.

In another embodiment, the invention features a method for the treatment of a patient having a condition associated with HBV and/or HCV infection, comprising contacting cells of said patient with an enzymatic nucleic acid molecule of the invention and further comprising the use of one or more drug therapies, for example, type I interferon or 3TC® (lamivudine), under conditions suitable for said treatment. In another embodiment, the other therapy is administered simultaneously with or separately from the enzymatic nucleic acid molecule.

In another embodiment, the invention features a method for inhibiting HBV and/or HCV replication in a mammalian cell comprising administering to the cell an enzymatic nucleic acid molecule of the invention under conditions suitable for the inhibition.

In yet another embodiment, the invention features a method of cleaving a separate HBV and/or HCV RNA comprising contacting an enzymatic nucleic acid molecule of the invention with the separate RNA under conditions suitable for the cleavage of the separate RNA.

In one embodiment, cleavage by an enzymatic nucleic acid molecule of the invention is carried out in the presence of a divalent cation, for example Mg^{2+} .

In another embodiment, the enzymatic nucleic acid molecule of the invention is chemically synthesized.

In another embodiment, the type I interferon contemplated by the invention is interferon alpha, interferon beta, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon.

In one embodiment, the invention features a composition comprising type I interferon and an enzymatic nucleic acid molecule of the invention and a pharmaceutically acceptable carrier.

In another embodiment, the invention features a method of administering to a cell, for example a mammalian cell or human cell, an enzymatic nucleic acid molecule of the

invention independently or in conjunction with other therapeutic compounds, such as type I interferon or 3TC® (lamivudine), comprising contacting the cell with the enzymatic nucleic acid molecule under conditions suitable for the administration.

In another embodiment, administration of an enzymatic nucleic acid molecule of the invention is in the presence of a delivery reagent, for example a lipid, cationic lipid, phospholipid, or liposome.

In another embodiment, the invention features novel nucleic acid-based techniques such as enzymatic nucleic acid molecules and antisense molecules and methods for their use to down regulate or inhibit the expression of HBV RNA and/or replication of HBV.

In another embodiment, the invention features novel nucleic acid-based techniques such as enzymatic nucleic acid molecules and antisense molecules and methods for their use to down regulate or inhibit the expression of HCV RNA and/or replication of HCV.

In one embodiment, the invention features the use of one or more of the enzymatic nucleic acid-based techniques to down-regulate or inhibit the expression of the genes encoding HBV and/or HCV viral proteins. Specifically, the invention features the use of enzymatic nucleic acid-based techniques to specifically down-regulate or inhibit the expression of the HBV and/or HCV viral genome.

In another embodiment, the invention features nucleic acid-based inhibitors (*e.g.*, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, decoys, siRNA, aptamers, and antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or inhibit the expression of RNA (*e.g.*, HBV and/or HCV) capable of progression and/or maintenance of hepatitis, hepatocellular carcinoma, cirrhosis, and/or liver failure.

In one embodiment, nucleic acid molecules of the invention are used to treat HBV infected cells or an HBV infected patient wherein the HBV is resistant or the patient does not respond to treatment with 3TC® (Lamivudine), either alone or in combination with other therapies under conditions suitable for the treatment.

In yet another embodiment, the invention features the use of an enzymatic nucleic acid molecule, preferably in the hammerhead, NCH (Inozyme), G-cleaver, amberzyme, zinzyme, and/or DNAzyme motif, to inhibit the expression of HBV and/or HCV RNA.

The enzymatic nucleic acid molecules described herein exhibit a high degree of specificity for only the viral mRNA in infected cells. Nucleic acid molecules of the instant invention targeted to highly conserved sequence regions allow the treatment of many strains

of human HBV and/or HCV with a single compound. No treatment presently exists which specifically attacks expression of the viral gene(s) that are responsible for transformation of hepatocytes by HBV and/or HCV.

The enzymatic nucleic acid-based modulators of HBV and HCV expression are useful for the prevention of the diseases and conditions including HBV and HCV infection, hepatitis, cancer, cirrhosis, liver failure, and any other diseases or conditions that are related to the levels of HBV and/or HCV in a cell or tissue.

Preferred target sites are genes required for viral replication, a non-limiting example includes genes for protein synthesis, such as the 5' most 1500 nucleotides of the HBV pregenomic mRNAs. For sequence references, see Renbao *et al.*, 1987, *Sci. Sin.*, 30, 507. This region controls the translational expression of the core protein (C), X protein (X) and DNA polymerase (P) genes and plays a role in the replication of the viral DNA by serving as a template for reverse transcriptase. Disruption of this region in the RNA results in deficient protein synthesis as well as incomplete DNA synthesis (and inhibition of transcription from the defective genomes). Targeting sequences 5' of the encapsidation site can result in the inclusion of the disrupted 3' RNA within the core virion structure and targeting sequences 3' of the encapsidation site can result in the reduction in protein expression from both the 3' and 5' fragments.

Alternative regions outside of the 5' most 1500 nucleotides of the pregenomic mRNA also make suitable targets for enzymatic nucleic acid mediated inhibition of HBV replication. Such targets include the mRNA regions that encode the viral S gene. Selection of particular target regions will depend upon the secondary structure of the pregenomic mRNA. Targets in the minor mRNAs can also be used, especially when folding or accessibility assays in these other RNAs reveal additional target sequences that are unavailable in the pregenomic mRNA species.

A desirable target in the pregenomic RNA is a proposed bipartite stem-loop structure in the 3'-end of the pregenomic RNA which is believed to be critical for viral replication (Kidd and Kidd-Ljunggren, 1996. *Nuc. Acid Res.* 24:3295-3302). The 5' end of the HBV pregenomic RNA carries a *cis*-acting encapsidation signal, which has inverted repeat sequences that are thought to form a bipartite stem-loop structure. Due to a terminal redundancy in the pregenomic RNA, the putative stem-loop also occurs at the 3'-end. While it is the 5' copy which functions in polymerase binding and encapsidation, reverse transcription actually begins from the 3' stem-loop. To start reverse transcription, a 4 nt primer which is covalently attached to the polymerase is made, using a bulge in the 5' encapsidation signal as template. This primer is then shifted, by an unknown mechanism, to the DR1 primer binding site in the 3' stem-loop structure, and reverse transcription proceeds

from that point. The 3' stem-loop, and especially the DR1 primer binding site, appear to be highly effective targets for ribozyme intervention.

Sequences of the pregenomic RNA are shared by the mRNAs for surface, core, polymerase, and X proteins. Due to the overlapping nature of the HBV transcripts, all share a common 3'-end. Enzymatic nucleic acids targeting of this common 3'-end will thus cleave the pregenomic RNA as well as all of the mRNAs for surface, core, polymerase and X proteins.

At least seven basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds in *trans* (and thus can cleave other RNA molecules) under physiological conditions. **Table I** summarizes some of the characteristics of these enzymatic RNA molecules. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets. Thus, a single enzymatic nucleic acid molecule is able to cleave many molecules of target RNA. In addition, the enzymatic nucleic acid is a highly specific inhibitor of gene expression, with the specificity of inhibition depending not only on the base-pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of an enzymatic nucleic acid molecule.

The enzymatic nucleic acid molecules that cleave the specified sites in HBV-specific RNAs represent a novel therapeutic approach to treat a variety of pathologic indications, including, HBV infection, hepatitis, hepatocellular carcinoma, tumorigenesis, cirrhosis, liver failure and other conditions related to the level of HBV.

In one of the preferred embodiments of the inventions described herein, the enzymatic nucleic acid molecule is formed in a hammerhead or hairpin motif, but can also be formed in the motif of a hepatitis delta virus, group I intron, group II intron or RNase P RNA (in association with an RNA guide sequence), *Neurospora* VS RNA, DNAzymes, NCH cleaving motifs, or G-cleavers. Examples of such hammerhead motifs are described by Dreyfus, *supra*, Rossi *et al.*, 1992, *AIDS Research and Human Retroviruses* 8, 183. Examples of hairpin motifs are described by Hampel *et al.*, EP0360257, Hampel and Tritz, 1989

Biochemistry 28, 4929, Feldstein *et al.*, 1989, *Gene* 82, 53, Haseloff and Gerlach, 1989, *Gene*, 82, 43, Hampel *et al.*, 1990 *Nucleic Acids Res.* 18, 299; and Chowrira & McSwiggen, US. Patent No. 5,631,359. The hepatitis delta virus motif is described by Perrotta and Been, 1992 *Biochemistry* 31, 16. The RNase P motif is described by Guerrier-Takada *et al.*, 1983 *Cell* 35, 849; Forster and Altman, 1990, *Science* 249, 783; and Li and Altman, 1996, *Nucleic Acids Res.* 24, 835. The *Neurospora* VS RNA ribozyme motif is described by Collins (Saville and Collins, 1990 *Cell* 61, 685-696; Saville and Collins, 1991 *Proc. Natl. Acad. Sci. USA* 88, 8826-8830; Collins and Olive, 1993 *Biochemistry* 32, 2795-2799; and Guo and Collins, 1995, *EMBO. J.* 14, 363). Group II introns are described by Griffin *et al.*, 1995, *Chem. Biol.* 2, 761; Michels and Pyle, 1995, *Biochemistry* 34, 2965; and Pyle *et al.*, International PCT Publication No. WO 96/22689. The Group I intron is described by Cech *et al.*, U.S. Patent 4,987,071. DNAzymes are described by Usman *et al.*, International PCT Publication No. WO 95/11304; Chartrand *et al.*, 1995, *NAR* 23, 4092; Breaker *et al.*, 1995, *Chem. Bio.* 2, 655; and Santoro *et al.*, 1997, *PNAS* 94, 4262. NCH cleaving motifs are described in Ludwig & Sproat, International PCT Publication No. WO 98/58058; and G-cleavers are described in Kore *et al.*, 1998, *Nucleic Acids Research* 26, 4116-4120 and Eckstein *et al.*, International PCT Publication No. WO 99/16871. Additional motifs include the Aptazyme (Breaker *et al.*, WO 98/43993), Amberzyme (Class I motif, **Figure 3**; Beigelman *et al.*, International PCT publication No. WO 99/55857) and Zinzyme (Beigelman *et al.*, International PCT publication No. WO 99/55857), all these references are incorporated by reference herein in their totalities, including drawings and can also be used in the present invention. These specific motifs are not limiting in the invention and those skilled in the art will recognize that all that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule (Cech *et al.*, U.S. Patent No. 4,987,071).

In preferred embodiments of the present invention, a nucleic acid molecule, *e.g.*, an antisense molecule, a triplex DNA, or a ribozyme, is 13 to 100 nucleotides in length, *e.g.*, in specific embodiments 35, 36, 37, or 38 nucleotides in length (*e.g.*, for particular ribozymes or antisense). In particular embodiments, the nucleic acid molecule is 15-100, 17-100, 20-100, 21-100, 23-100, 25-100, 27-100, 30-100, 32-100, 35-100, 40-100, 50-100, 60-100, 70-100, or 80-100 nucleotides in length. Instead of 100 nucleotides being the upper limit on the length ranges specified above, the upper limit of the length range can be, for example, 30, 40, 50, 60, 70, or 80 nucleotides. Thus, for any of the length ranges, the length range for particular embodiments has lower limit as specified, with an upper limit as specified which is greater than the lower limit. For example, in a particular embodiment, the length range can be 35-50 nucleotides in length. All such ranges are expressly included. Also in particular

embodiments, a nucleic acid molecule can have a length which is any of the lengths specified above, for example, 21 nucleotides in length.

Exemplary enzymatic nucleic acid molecules of the invention targeting HBV are shown in **Tables V-XI**. For example, enzymatic nucleic acid molecules of the invention are preferably between 15 and 50 nucleotides in length, more preferably between 25 and 40 nucleotides in length, *e.g.*, 34, 36, or 38 nucleotides in length (for example see Jarvis *et al.*, 1996, *J. Biol. Chem.*, 271, 29107-29112). Exemplary DNAzymes of the invention are preferably between 15 and 40 nucleotides in length, more preferably between 25 and 35 nucleotides in length, *e.g.*, 29, 30, 31, or 32 nucleotides in length (see for example Santoro *et al.*, 1998, *Biochemistry*, 37, 13330-13342; Chartrand *et al.*, 1995, *Nucleic Acids Research*, 23, 4092-4096). Exemplary antisense molecules of the invention are preferably between 15 and 75 nucleotides in length, more preferably between 20 and 35 nucleotides in length, *e.g.*, 25, 26, 27, or 28 nucleotides in length (see for example Woolf *et al.*, 1992, *PNAS*, 89, 7305-7309; Milner *et al.*, 1997, *Nature Biotechnology*, 15, 537-541). Exemplary triplex forming oligonucleotide molecules of the invention are preferably between 10 and 40 nucleotides in length, more preferably between 12 and 25 nucleotides in length, *e.g.*, 18, 19, 20, or 21 nucleotides in length (see for example Maher *et al.*, 1990, *Biochemistry*, 29, 8820-8826; Strobel and Dervan, 1990, *Science*, 249, 73-75). Those skilled in the art will recognize that all that is required is for the nucleic acid molecule are of length and conformation sufficient and suitable for the nucleic acid molecule to catalyze a reaction contemplated herein. The length of the nucleic acid molecules of the instant invention are not limiting within the general limits stated.

In a preferred embodiment, the invention provides a method for producing a class of nucleic acid-based gene inhibiting agents which exhibit a high degree of specificity for the RNA of a desired target. For example, the enzymatic nucleic acid molecule is preferably targeted to a highly conserved sequence region of target RNAs encoding HBV proteins (specifically HBV RNA) such that specific treatment of a disease or condition can be provided with either one or several nucleic acid molecules of the invention. Such nucleic acid molecules can be delivered exogenously to specific tissue or cellular targets as required. Alternatively, the nucleic acid molecules (*e.g.*, ribozymes and antisense) can be expressed from DNA and/or RNA vectors that are delivered to specific cells.

The enzymatic nucleic acid-based inhibitors of HBV expression are useful for the prevention of the diseases and conditions including HBV infection, hepatitis, cancer, cirrhosis, liver failure, and any other diseases or conditions that are related to the levels of HBV in a cell or tissue.

The nucleic acid-based inhibitors of the invention are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells or tissues. The nucleic acid or nucleic acid complexes can be locally administered to relevant tissues *ex vivo*, or *in vivo* through injection, infusion pump or stent, with or without their incorporation in biopolymers. In preferred embodiments, the enzymatic nucleic acid HBV inhibitors comprise sequences, which are complementary to the substrate sequences in. Examples of such enzymatic nucleic acid molecules also are shown in. Examples of such enzymatic nucleic acid molecules consist essentially of sequences defined in these tables.

In yet another embodiment, the invention features antisense nucleic acid molecules including sequences complementary to the HBV substrate sequences shown in. Such nucleic acid molecules can include sequences as shown for the binding arms of the enzymatic nucleic acid molecules in. Similarly, triplex molecules can be provided targeted to the corresponding DNA target regions, and regions containing the DNA equivalent of a target sequence or a sequence complementary to the specified target (substrate) sequence. Typically, antisense molecules are complementary to a target sequence along a single contiguous sequence of the antisense molecule. However, in certain embodiments, an antisense molecule can bind to substrate such that the substrate molecule forms a loop, and/or an antisense molecule can bind such that the antisense molecule forms a loop. Thus, the antisense molecule can be complementary to two (or even more) non-contiguous substrate sequences or two (or even more) non-contiguous sequence portions of an antisense molecule can be complementary to a target sequence or both.

By "consists essentially of" is meant that the active nucleic acid molecule of the invention, for example, an enzymatic nucleic acid molecule, contains an enzymatic center or core equivalent to those in the examples, and binding arms able to bind RNA such that cleavage at the target site occurs. Other sequences can be present which do not interfere with such cleavage. Thus, a core region can, for example, include one or more loops, stem-loop structure, or linker which does not prevent enzymatic activity. Thus, the underlined regions in the sequences in can be such a loop, stem-loop, nucleotide linker, and/or non-nucleotide linker and can be represented generally as sequence "X". For example, a core sequence for a hammerhead enzymatic nucleic acid can comprise a conserved sequence, such as 5'-CUGAUGAG-3' and 5'-CGAA-3' connected by "X", where X is 5'-GCCGUUAGGC-3' (SEQ ID NO. 16201), or any other Stem II region known in the art, or a nucleotide and/or non-nucleotide linker. Similarly, for other nucleic acid molecules of the instant invention, such as Inozyme, G-cleaver, amberzyme, zinzyme, DNAzyme, antisense, 2-5A antisense, triplex forming nucleic acid, and decoy nucleic acids, other sequences or non-nucleotide linkers can be present that do not interfere with the function of the nucleic acid molecule.

In another aspect of the invention, enzymatic nucleic acids or antisense molecules that interact with target RNA molecules and inhibit HBV (specifically HBV RNA) activity are expressed from transcription units inserted into DNA or RNA vectors. The recombinant vectors are preferably DNA plasmids or viral vectors. Enzymatic nucleic acid or antisense expressing viral vectors can be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, the recombinant vectors capable of expressing the enzymatic nucleic acids or antisense are delivered as described above, and persist in target cells. Alternatively, viral vectors can be used that provide for transient expression of enzymatic nucleic acids or antisense. Such vectors can be repeatedly administered as necessary. Once expressed, the enzymatic nucleic acids or antisense bind to the target RNA and inhibit its function or expression. Delivery of enzymatic nucleic acids or antisense expressing vectors can be systemic, such as by intravenous or intramuscular administration, by administration to target cells ex-planted from the patient followed by reintroduction into the patient, or by any other means that allow for introduction into the desired target cell. Antisense DNA can be expressed via the use of a single stranded DNA intracellular expression vector.

In another embodiment, the invention features nucleic acid-based inhibitors (*e.g.*, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, decoys, aptamers, siRNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or inhibit the expression of RNA (*e.g.*, HBV) capable of progression and/or maintenance of liver disease and failure.

In another embodiment, the invention features nucleic acid-based techniques (*e.g.*, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, decoys, aptamers, siRNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or inhibit the expression of HBV RNA expression.

In other embodiments, the invention features a method for the analysis of HBV proteins. This method is useful in determining the efficacy of HBV inhibitors. Specifically, the instant invention features an assay for the analysis of HBsAg proteins and secreted alkaline phosphatase (SEAP) control proteins to determine the efficacy of agents used to modulate HBV expression.

The method consists of coating a micro-titer plate with an antibody such as anti-HBsAg Mab (for example, Biostride B88-95-31ad,ay) at 0.1 to 10 $\mu\text{g/ml}$ in a buffer (for example, carbonate buffer, such as Na_2CO_3 15 mM, NaHCO_3 35 mM, pH 9.5) at 4°C overnight. The microtiter wells are then washed with PBST or the equivalent thereof, (for example, PBS, 0.05% Tween 20) and blocked for 0.1-24 hr at 37° C with PBST, 1% BSA or the equivalent thereof. Following washing as above, the wells are dried (for example, at 37° C for 30 min).

Biotinylated goat anti-HBsAg or an equivalent antibody (for example, Accurate YVS1807) is diluted (for example at 1:1000) in PBST and incubated in the wells (for example, 1 hr. at 37° C). The wells are washed with PBST (for example, 4x). A conjugate, (for example, Streptavidin/Alkaline Phosphatase Conjugate, Pierce 21324) is diluted to 10-10,000 ng/ml in PBST, and incubated in the wells (for example, 1 hr. at 37° C). After washing as above, a substrate (for example, p-nitrophenyl phosphate substrate, Pierce 37620) is added to the wells, which are then incubated (for example, 1 hr. at 37° C). The optical density is then determined (for example, at 405 nm). SEAP levels are then assayed, for example, using the Great EscAPe® Detection Kit (Clontech K2041-1), as per the manufacturers instructions. In the above example, incubation times and reagent concentrations can be varied to achieve optimum results, a non-limiting example is described in Example 6.

Comparison of this HBsAg ELISA method to a commercially available assay from World Diagnostics, Inc. 15271 NW 60th Ave, #201, Miami Lakes, FL 33014 (305) 827-3304 (Cat. No. EL10018) demonstrates an increase in sensitivity (signal:noise) of 3-20 fold.

This invention also relates to nucleic acid molecules directed to disrupt the function of HBV reverse transcriptase. In addition, the invention relates to nucleic acid molecules directed to disrupt the function of the Enhancer I core region of the HBV genomic DNA. In particular, the present invention describes the selection and function of nucleic acid molecules, such as decoys and aptamers, capable of specifically binding to the HBV reverse transcriptase (pol) primer and modulating reverse transcription of the HBV pregenomic RNA. In another embodiment, the present invention relates to nucleic acid molecules, such as decoys, antisense and aptamers, capable of specifically binding to the HBV reverse transcriptase (pol) and modulating reverse transcription of the HBV pregenomic RNA. In yet another embodiment, the present invention relates to nucleic acid molecules capable of specifically binding to the HBV Enhancer I core region and modulating transcription of the HBV genomic DNA. The invention further relates to allosteric enzymatic nucleic acid molecules or "allozymes" that are used to modulate HBV gene expression. Such allozymes are active in the presence of HBV-derived nucleic acids, peptides, and/or proteins such as HBV reverse transcriptase and/or a HBV reverse transcriptase primer sequence, thereby allowing the allozyme to selectively cleave a sequence of HBV DNA or RNA. Allozymes of the invention are also designed to be active in the presence of HBV Enhancer I sequences and/or mutant HBV Enhancer I sequences, thereby allowing the allozyme to selectively cleave a sequence of HBV DNA or RNA. These nucleic acid molecules can be used to treat diseases and disorders associated with HBV infection.

In one embodiment, the invention features a nucleic acid decoy molecule that specifically binds the hepatitis B virus (HBV) reverse transcriptase primer sequence. In

another embodiment, the invention features a nucleic acid decoy molecule that specifically binds the hepatitis B virus (HBV) reverse transcriptase. In yet another embodiment, the invention features a nucleic acid decoy molecule that specifically binds to the HBV Enhancer I core sequence.

In one embodiment, the invention features a nucleic acid aptamer that specifically binds the hepatitis B virus (HBV) reverse transcriptase primer. In another embodiment, the invention features a nucleic acid aptamer that specifically binds the hepatitis B virus (HBV) reverse transcriptase. In yet another embodiment, the invention features a nucleic acid aptamer molecule that specifically binds to the HBV Enhancer I core sequence.

In one embodiment, the invention features an allozyme that specifically binds the hepatitis B virus (HBV) reverse transcriptase primer. In another embodiment, the invention features an allozyme that specifically binds the hepatitis B virus (HBV) reverse transcriptase. In yet another embodiment, the invention features an allozyme that specifically binds to the HBV Enhancer I core sequence.

In yet another embodiment, the invention features a nucleic acid molecule, for example a triplex forming nucleic acid molecule or antisense nucleic acid molecule, that binds the hepatitis B virus (HBV) reverse transcriptase primer. In another embodiment, the invention features a triplex forming nucleic acid molecule or antisense nucleic acid molecule that specifically binds the hepatitis B virus (HBV) reverse transcriptase. In yet another embodiment, the invention features a triplex forming nucleic acid molecule or antisense nucleic acid molecule that specifically binds to the HBV Enhancer I core sequence.

In another embodiment, a nucleic acid molecule of the invention binds to Hepatocyte Nuclear Factor 3 (HNF3) and/or Hepatocyte Nuclear Factor 4 (HNF4) binding sequence within the HBV Enhancer I region of HBV genomic DNA, for example the plus strand and/or minus strand DNA of the Enhancer I region, and blocks the binding of HNF3 and/or HNF4 to the Enhancer I region.

In another embodiment, the nucleic acid molecule of the invention comprises a sequence having $(UUC A)_n$ domain, where n is an integer from 1-10. In another embodiment, the nucleic acid molecules of the invention comprise the sequence of SEQ. ID NOs: 11216 - 11342.

In another embodiment, the invention features a composition comprising a nucleic acid molecule of the invention and a pharmaceutically acceptable carrier. In another embodiment, the invention features a mammalian cell, for example a human cell, including a nucleic acid molecule contemplated by the invention.

In one embodiment, the invention features a method for treatment of HBV infection, cirrhosis, liver failure, or hepatocellular carcinoma, comprising administering to a patient a nucleic acid molecule of the invention under conditions suitable for the treatment.

In another embodiment, the invention features a method for the treatment of a patient having a condition associated with HBV infection comprising contacting cells of said patient with a nucleic acid molecule of the invention under conditions suitable for such treatment. In another embodiment, the invention features a method for the treatment of a patient having a condition associated with HBV infection comprising contacting cells of said patient with a nucleic acid molecule of the invention, and further comprising the use of one or more drug therapies, for example type I interferon or 3TC® (lamivudine), under conditions suitable for said treatment. In another embodiment, the other therapy is administered simultaneously with or separately from the nucleic acid molecule.

In another embodiment, the invention features a method for modulating HBV replication in a mammalian cell comprising administering to the cell a nucleic acid molecule of the invention under conditions suitable for the modulation.

In yet another embodiment, the invention features a method of modulating HBV reverse transcriptase activity comprising contacting a nucleic acid molecule of the invention, for example a decoy or aptamer, with HBV reverse transcriptase under conditions suitable for the modulating of the HBV reverse transcriptase activity.

In another embodiment, the invention features a method of modulating HBV transcription comprising contacting a nucleic molecule of the invention with a HBV Enhancer I sequence under conditions suitable for the modulation of HBV transcription.

In one embodiment, a nucleic acid molecule of the invention, for example a decoy or aptamer, is chemically synthesized. In another embodiment, the nucleic acid molecule of the invention comprises at least one nucleic acid sugar modification. In yet another embodiment, the nucleic acid molecule of the invention comprises at least one nucleic acid base modification. In another embodiment, the nucleic acid molecule of the invention comprises at least one nucleic acid backbone modification.

In another embodiment, the nucleic acid molecule of the invention comprises at least one 2'-O-alkyl, 2'-alkyl, 2'-alkoxylalkyl, 2'-alkylthioalkyl, 2'-amino, 2'-O-amino, or 2'-halo modification and/or any combination thereof with or without 2'-deoxy and/or 2'-ribo nucleotides. In yet another embodiment, the nucleic acid molecule of the invention comprises all 2'-O-alkyl nucleotides, for example, all 2'-O-allyl nucleotides.

In one embodiment, the nucleic acid molecule of the invention comprises a 5'-cap, 3'-cap, or 5'-3' cap structure, for example an abasic or inverted abasic moiety.

In another embodiment, the nucleic acid molecule of the invention is a linear nucleic acid molecule. In another embodiment, the nucleic acid molecule of the invention is a linear nucleic acid molecule that can optionally form a hairpin, loop, stem-loop, or other secondary structure. In yet another embodiment, the nucleic acid molecule of the invention is a circular nucleic acid molecule.

In one embodiment, the nucleic acid molecule of the invention is a single stranded oligonucleotide. In another embodiment, the nucleic acid molecule of the invention is a double-stranded oligonucleotide.

In one embodiment, the nucleic acid molecule of the invention comprises an oligonucleotide having between about 3 and about 100 nucleotides. In another embodiment, the nucleic acid molecule of the invention comprises an oligonucleotide having between about 3 and about 24 nucleotides. In another embodiment, the nucleic acid molecule of the invention comprises an oligonucleotide having between about 4 and about 16 nucleotides.

The nucleic acid decoy molecules and/or aptamers that bind to a reverse transcriptase and/or reverse transcriptase primer and therefore inactivate the reverse transcriptase, represent a novel therapeutic approach to treat a variety of pathologic indications, including, viral infection such as HBV infection, hepatitis, hepatocellular carcinoma, tumorigenesis, cirrhosis, liver failure and others.

The nucleic acid molecules that bind to a HBV Enhancer I sequence and therefore inactivate HBV transcription, represent a novel therapeutic approach to treat a variety of pathologic indications, including viral infection such as HBV infection, hepatitis, hepatocellular carcinoma, tumorigenesis, cirrhosis, liver failure and others conditions associated with the level of HBV.

In one embodiment of the present invention, a decoy nucleic acid molecule of the invention is 4 to 50 nucleotides in length, in specific embodiments about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 nucleotides in length. In another embodiment, a non-decoy nucleic acid molecule, *e.g.*, an antisense molecule, a triplex DNA, or a ribozyme, is 13 to 100 nucleotides in length, *e.g.*, in specific embodiments 35, 36, 37, or 38 nucleotides in length (*e.g.*, for particular ribozymes or antisense). In particular embodiments, the nucleic acid molecule is 15-100, 17-100, 20-100, 21-100, 23-100, 25-100, 27-100, 30-100, 32-100, 35-100, 40-100, 50-100, 60-100, 70-100, or 80-100 nucleotides in length. Instead of 100 nucleotides being the upper limit on the length ranges specified above, the upper limit of the

length range can be, for example, 30, 40, 50, 60, 70, or 80 nucleotides. Thus, for any of the length ranges, the length range for particular embodiments has lower limit as specified, with an upper limit as specified which is greater than the lower limit. For example, in a particular embodiment, the length range can be 35-50 nucleotides in length. All such ranges are expressly included. Also in particular embodiments, a nucleic acid molecule can have a length which is any of the lengths specified above, for example, 21 nucleotides in length.

Exemplary nucleic acid decoy molecules of the invention are shown in Table XIV. Exemplary synthetic nucleic acid molecules of the invention are shown in Table XV. For example, decoy molecules of the invention are between 4 and 40 nucleotides in length. Exemplary decoys of the invention are 4, 8, 12, or 16 nucleotides in length. In an additional example, enzymatic nucleic acid molecules of the invention are preferably between 15 and 50 nucleotides in length, more preferably between 25 and 40 nucleotides in length, *e.g.*, 34, 36, or 38 nucleotides in length (for example see Jarvis *et al.*, 1996, *J. Biol. Chem.*, 271, 29107-29112). Exemplary DNAzymes of the invention are preferably between 15 and 40 nucleotides in length, more preferably between 25 and 35 nucleotides in length, *e.g.*, 29, 30, 31, or 32 nucleotides in length (see for example Santoro *et al.*, 1998, *Biochemistry*, 37, 13330-13342; Chartrand *et al.*, 1995, *Nucleic Acids Research*, 23, 4092-4096). Exemplary antisense molecules of the invention are preferably between 15 and 75 nucleotides in length, more preferably between 20 and 35 nucleotides in length, *e.g.*, 25, 26, 27, or 28 nucleotides in length (see for example Woolf *et al.*, 1992, *PNAS.*, 89, 7305-7309; Milner *et al.*, 1997, *Nature Biotechnology*, 15, 537-541). Exemplary triplex forming oligonucleotide molecules of the invention are preferably between 10 and 40 nucleotides in length, more preferably between 12 and 25 nucleotides in length, *e.g.*, 18, 19, 20, or 21 nucleotides in length (see for example Maher *et al.*, 1990, *Biochemistry*, 29, 8820-8826; Strobel and Dervan, 1990, *Science*, 249, 73-75). Those skilled in the art will recognize that all that is required is that the nucleic acid molecule is of length and conformation sufficient and suitable for the nucleic acid molecule to catalyze a reaction contemplated herein. The length of the nucleic acid molecules of the instant invention are not limiting within the general limits stated.

In one embodiment, the invention provides a method for producing a class of nucleic acid-based gene modulating agents, which exhibit a high degree of specificity for a viral reverse transcriptase such as HBV reverse transcriptase or reverse transcriptase primer such as a HBV reverse transcriptase primer. For example, the nucleic acid molecule is preferably targeted to a highly conserved nucleic acid binding region of the viral reverse transcriptase such that specific treatment of a disease or condition can be provided with either one or several nucleic acid molecules of the invention. Such nucleic acid molecules can be delivered exogenously to specific tissue or cellular targets as required. Alternatively, the

nucleic acid molecules can be expressed from DNA and/or RNA vectors that are delivered to specific cells.

In another embodiment, the invention provides a method for producing a class of nucleic acid-based gene modulating agents which exhibit a high degree of specificity for a viral enhancer regions such as the HBV Enhancer I core sequence. For example, the nucleic acid molecule is preferably targeted to a highly conserved transcription factor-binding region of the viral Enhancer I sequence such that specific treatment of a disease or condition can be provided with either one or several nucleic acid molecules of the invention. Such nucleic acid molecules can be delivered exogenously to specific tissue or cellular targets as required. Alternatively, the nucleic acid molecules can be expressed from DNA and/or RNA vectors that are delivered to specific cells.

In a another embodiment the invention provides a method for producing a class of enzymatic cleaving agents which exhibit a high degree of specificity for the RNA of a desired target. The enzymatic nucleic acid molecule, nuclease activating compound or chimera is preferably targeted to a highly conserved sequence region of a target mRNAs encoding HCV or HBV proteins such that specific treatment of a disease or condition can be provided with either one or several enzymatic nucleic acids. Such nucleic acid molecules can be delivered exogenously to specific cells as required. Alternatively, the enzymatic nucleic acid molecules can be expressed from DNA/RNA vectors that are delivered to specific cells. DNAzymes can be synthesized chemically or expressed endogenously *in vivo*, by means of a single stranded DNA vector or equivalent thereof.

In another embodiment, the nucleic acid molecule of the invention binds irreversibly to the HBV reverse transcriptase target, for example by covalent attachment of the nucleic molecule to the reverse transcriptase primer sequence. The covalent attachment can be accomplished by introducing chemical modifications into the nucleic acid molecule's (for example, decoy or aptamer) sequence that are capable of forming covalent bonds to the reverse transcriptase primer sequence.

In another embodiment, the nucleic acid molecule of the invention binds irreversibly to the HBV Enhancer I sequence target, for example, by covalent attachment of the nucleic acid molecule to the HBV Enhancer I sequence. The covalent attachment can be accomplished by introducing chemical modifications into the nucleic acid molecule's sequence that are capable of forming covalent bonds to the reverse transcriptase primer sequence.

In another embodiment, the type I interferon contemplated by the invention is interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon,

polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon.

In one embodiment, the invention features a composition comprising type I interferon and a nucleic acid molecule of the invention and a pharmaceutically acceptable carrier.

In another embodiment, the invention features a method of administering to a cell, for example a mammalian cell or human cell, a nucleic acid molecule of the invention independently or in conjunction with other therapeutic compounds, such as type I interferon or 3TC® (lamivudine), comprising contacting the cell with the nucleic acid molecule under conditions suitable for the administration.

In yet another embodiment, the invention features a method of administering to a cell, for example a mammalian cell or human cell, a nucleic acid molecule of the invention independently or in conjunction with other therapeutic compounds such as enzymatic nucleic acid molecules, antisense molecules, triplex forming oligonucleotides, 2,5-A chimeras, and/or RNAi, comprising contacting the cell with the nucleic acid molecule of the invention under conditions suitable for the administration.

In another embodiment, administration of a nucleic acid molecule of the invention is administered to a cell or patient in the presence of a delivery reagent, for example a lipid, cationic lipid, phospholipid, or liposome.

In one embodiment, the invention features novel nucleic acid-based techniques such as nucleic acid decoy molecules and/or aptamers, used alone or in combination with enzymatic nucleic acid molecules, antisense molecules, and/or RNAi, and methods for use to down regulate or modulate the expression of HBV RNA and/or replication of HBV.

In another embodiment, the invention features the use of one or more of the nucleic acid-based techniques to modulate the expression of the genes encoding HBV viral proteins. Specifically, the invention features the use of nucleic acid-based techniques to specifically modulate the expression of the HBV viral genome.

In another embodiment, the invention features the use of one or more of the nucleic acid-based techniques to modulate the activity, expression, or level of cellular proteins required for HBV replication. For example, the invention features the use of nucleic acid-based techniques to specifically modulate the activity of cellular proteins required for HBV replication.

In another embodiment, the invention features nucleic acid-based modulators (e.g., nucleic acid decoy molecules, aptamers, enzymatic nucleic acid molecules (ribozymes),

antisense nucleic acids, triplex DNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or modulate reverse transcriptase activity and/or the expression of RNA (*e.g.*, HBV) capable of progression and/or maintenance of HBV infection, hepatocellular carcinoma, liver disease and failure.

In another embodiment, the invention features nucleic acid-based techniques (*e.g.*, nucleic acid decoy molecules, aptamers, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acid molecules, triplex DNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or modulate reverse transcriptase activity and/or the expression of HBV RNA.

In another embodiment, the invention features nucleic acid-based modulators (*e.g.*, nucleic acid decoy molecules, aptamers, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, siRNA, dsRNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or modulate Enhancer I mediated transcription activity and/or the expression of DNA (*e.g.*, HBV) capable of progression and/or maintenance of HBV infection, hepatocellular carcinoma, liver disease and failure.

In another embodiment, the invention features nucleic acid-based techniques (*e.g.*, nucleic acid decoy molecules, aptamers, enzymatic nucleic acid molecules, antisense nucleic acid molecules, triplex DNA, siRNA, antisense nucleic acids containing DNA cleaving chemical groups) and methods for their use to down regulate or modulate Enhancer I mediated transcription activity and/or the expression of HBV DNA.

In another embodiment, the invention features a nucleic acid sensor molecule having an enzymatic nucleic acid domain and a sensor domain that interacts with an HBV peptide, protein, or polynucleotide sequence, for example, HBV reverse transcriptase, HBV reverse transcriptase primer, or the Enhancer I element of the HBV pregenomic RNA, wherein such interaction results in modulation of the activity of the enzymatic nucleic acid domain of the nucleic acid sensor molecule. In another embodiment, the invention features HBV-specific nucleic acid sensor molecules or allozymes, and methods for their use to down regulate or modulate the expression of HBV RNA capable of progression and/or maintenance of hepatitis, hepatocellular carcinoma, cirrhosis, and/or liver failure. In yet another embodiment, the enzymatic nucleic acid domain of a nucleic acid sensor molecule of the invention is a Hammerhead, Inozyme, G-cleaver, DNazyme, Zinzyme, Amberzyme, or Hairpin enzymatic nucleic acid molecule.

In one embodiment, nucleic acid molecules of the invention are used to treat HBV-infected cells or a HBV-infected patient wherein the HBV is resistant or the patient does not

respond to treatment with 3TC® (Lamivudine), either alone or in combination with other therapies under conditions suitable for the treatment.

In another embodiment, nucleic acid molecules of the invention are used to treat HBV-infected cells or a HBV-infected patient, wherein the HBV is resistant or the patient does not respond to treatment with Interferon, for example Infergen®, either alone or in combination with other therapies under conditions suitable for the treatment.

The invention also relates to *in vitro* and *in vivo* systems, including, e.g., mammalian systems for screening inhibitors of HBV. In one embodiment, the invention features a mouse, for example a male or female mouse, implanted with HepG2.2.15 cells, wherein the mouse is susceptible to HBV infection and capable of sustaining HBV DNA expression. One embodiment of the invention provides a mouse implanted with HepG2.2.15 cells, wherein said mouse sustains the propagation of HEPG2.2.15 cells and HBV production.

In another embodiment, a mouse of the invention has been infected with HBV for at least one week to at least eight weeks, including, for example at least 4 weeks.

In yet another embodiment, a mouse of the invention, for example a male or female mouse, is an immunocompromised mouse, for example a nu/nu mouse or a scid/scid mouse.

In one embodiment, the invention features a method of producing a mouse of the invention, comprising injecting, for example by subcutaneous injection, HepG2.2.15 (Sells, *et al.*, 1987, *Proc Natl Acad Sci U S A.*, 84, 1005-1009) cells into the mouse under conditions suitable for the propagation of HepG2.2.15 cells in said mouse. HepG2.2.15 cells can be suspended in, for example, Delbecco's PBS solution including calcium and magnesium. In another embodiment, HepG2.2.15 cells are selected for antibiotic resistance and are then introduced into the mouse under conditions suitable for the propagation of HepG2.2.15 cells in said mouse. A non-limiting example of antibiotic resistant HepG2.2.15 cells include G418 antibiotic resistant HepG2.2.15 cells.

In another embodiment, the invention features a method of screening a compound for therapeutic activity against HBV, comprising administering the compound to a mouse of the invention and monitoring the levels of HBV produced (e.g. by assaying for HBV DNA levels) in the mouse.

In one embodiment, a therapeutic compound or therapy contemplated by the invention is a lipid, steroid, peptide, protein, antibody, monoclonal antibody, humanized monoclonal antibody, small molecule, and/or isomers and analogs thereof, and/or a cell.

In one embodiment, a therapeutic compound or therapy contemplated by the invention is a nucleic acid molecule, for example a nucleic acid molecule, such as an enzymatic nucleic acid molecule, antisense nucleic acid molecule, allozyme, peptide nucleic acid, decoy, triplex oligonucleotide, dsRNA, ssRNA, RNAi, siRNA, aptamer, or 2,5-A chimera used alone or in combination with another therapy, for example antiviral therapy. Antiviral therapy can be, for example, treatment with 3TC® (Lamivudine) or interferon. Interferon can include, for example, consensus interferon or type I interferon. Type I interferon can include interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, or polyethylene glycol consensus interferon.

In one embodiment, the invention features a non-human mammal implanted with HepG2.2.15 cells, wherein the non-human mammal is susceptible to HBV infection and capable of sustaining HBV DNA expression in the implanted HepG2.2.15 cells.

In another embodiment, a non-human mammal of the invention, for example a male or female non-human mammal, has been infected with HBV for at least one week to at least eight weeks, including for example at least four weeks.

In yet another embodiment, a non-human mammal of the invention is an immunocompromised mammal, for example a nu/nu mammal or a scid/scid mammal.

In one embodiment, the invention features a method of producing a non-human mammal comprising HepG2.2.15 cells comprising injecting, for example by subcutaneous injection, HepG2.2.15 cells into the non-human mammal under conditions suitable for the propagation of HepG2.2.15 cells in said non-human mammal.

In another embodiment, the invention features a method of screening a compound for therapeutic activity against HBV comprising administering the compound to a non-human mammal of the invention and monitoring the levels of HBV produced (e.g. by assaying for HBV DNA levels) in the non-human mammals.

In one embodiment, a therapeutic compound or therapy contemplated by the invention is a nucleic acid molecule, for example an enzymatic nucleic acid molecule, allozyme, antisense nucleic acid molecule, decoy, triplex oligonucleotide, dsRNA, ssRNA, RNAi, siRNA, or 2,5-A chimera used alone or in combination with another therapy, for example antiviral therapy.

Methods and chimeric immunocompromised heterologous non-human mammalian hosts, particularly mouse hosts, are provided for the expression of hepatitis B virus ("HBV").

In one embodiment, the chimeric hosts have transplanted viable, HepG2.2.15 cells in an immunocompromised host.

The non-human mammals contemplated by the invention are immunocompromised in normally inheriting the desired immune incapacity, or the desired immune incapacity can be created. For example, hosts with severe combined immunodeficiency, known as scid/scid hosts, are available. Rodentia, particularly mice, and equine, particularly horses, are presently available as scid/scid hosts, for example scid/scid mice and scid/scid rats. The scid/scid hosts lack functioning lymphocyte types, particularly B-cells and some T-cell types. In the scid/scid mouse hosts, the genetic defect appears to be a non-functioning recombinase, as the germline DNA is not rearranged to produce functioning surface immunoglobulin and T-cell receptors.

Any immunodeficient non-human mammals, e.g. mouse, can be used to generate the animal models described herein. The term "immunodeficient," as used herein, refers to a genetic alteration that impairs the animal's ability to mount an effective immune response. In this regard, an "effective immune response" is one which is capable of destroying invading pathogens such as (but not limited to) viruses, bacteria, parasites, malignant cells, and/or a xenogeneic or allogeneic transplant. In one embodiment, the immunodeficient mouse is a severe immunodeficient (SCID) mouse, which lacks recombinase activity that is necessary for the generation of immunoglobulin and functional T cell antigen receptors, and thus does not produce functional B and T lymphocytes. In another embodiment, the immunodeficient mouse is a nude mouse, which contains a genetic defect that results in the absence of a functional thymus, leading to T-cell and B-cell deficiencies. However, mice containing other immunodeficiencies (such as rag-1 or rag-2 knockouts, as described in Chen *et al.*, 1994, *Curr. Opin. Immunol.*, 6, 313-319 and Gidas *et al.*, 1995, *J. Exp. Med.*, 181, 1187-1195, or beige-nude mice, which also lack natural killer cells, as described in Kollmann *et al.*, 1993, *J. Exp. Med.*, 177, 821-832) can also be employed.

The introduction of HepG2.2.15 cells occurs with a host at an age less than about 25% of its normal lifespan, usually to 20% of the normal lifespan with mice, and the age will generally be of an age of about 3 to 10 weeks, more usually from about 4 to 8 weeks. The mice can be of either sex, can be neutered, and can be otherwise normal, except for the immunocompromised state, or they can have one or more mutations, which can be naturally occurring or as a result of mutagenesis.

In another embodiment, the mouse model described herein is used to evaluate the effectiveness of the therapeutic compounds and methods. The terms "therapeutic compounds", "therapeutic methods" and "therapy" as used herein, encompass exogenous factors, such as dietary or environmental conditions, as well as pharmaceutical compositions

“drugs” and vaccines. In one embodiment, the therapeutic method is an immunotherapy, which can include the treatment of the HBV bearing animal with populations of HBV-reactive immune cells. The therapeutic method can also, or alternatively, be a gene therapy (i.e., a therapy that involves treatment of the HBV-bearing mouse with a cell population that has been manipulated to express one or more genes, the products of which can possess anti-viral activity), see for example *The Development of Human Gene Therapy*, Theodore Friedmann, Ed. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1999. Therapeutic compounds of the invention can comprise a drug or composition with pharmaceutical activity that can be used to treat illness or disease. A therapeutic method can comprise the use of a plurality of compounds in a mixture or a distinct entity. Examples of such compounds include nucleosides, nucleic acids, nucleic acid chimeras, RNA and DNA oligonucleotides, peptide nucleic acids, enzymatic nucleic acid molecules, antisense nucleic acid molecules, decoys, triplex oligonucleotides, ssDNA, dsRNA, ssRNA, siRNA, 2,5-A chimeras, lipids, steroids, peptides, proteins, antibodies, monoclonal antibodies (see for example Hall, 1995, *Science*, 270, 915-916), small molecules, and/or isomers and analogs thereof.

The methods of this invention can be used to treat human hepatitis B virus infections, which include productive virus infection, latent or persistent virus infection, and HBV-induced hepatocyte transformation. The utility can be extended to other species of HBV that infect non-human animals where such infections are of veterinary importance.

Preferred binding sites of the nucleic acid molecules of the invention include, but are not limited, to the primer binding site on HBV reverse transcriptase, the primer binding sequences of the HBV RNA, and/or the HBV Enhancer I region of HBV DNA.

This invention further relates to nucleic acid molecules that target RNA species of hepatitis C virus (HCV) and/or encoded by the HCV. In one embodiment, applicant describes enzymatic nucleic acid molecules that specifically cleave HCV RNA and the selection and function thereof. The invention further relates to compounds and chimeric molecules comprising nuclease activating activity. The invention also relates to compositions and methods for the cleavage of RNA using these nuclease activating compounds and chimeras. Nucleic acid molecules, nuclease activating compounds and chimeras, and compositions and methods of the invention can be used to treat diseases associated with HCV infection.

Due to the high sequence variability of the HCV genome, selection of nucleic acid molecules and nuclease activating compounds and chimeras for broad therapeutic applications preferably involve the conserved regions of the HCV genome. Thus, in one embodiment the present invention describes nucleic acid molecules that cleave the conserved

regions of the HCV genome. The invention further describes compounds and chimeric molecules that activate cellular nucleases that cleave HCV RNA, including conserved regions of the HCV genome. Examples of conserved regions of the HCV genome include but are not limited to the 5'-Non Coding Region (NCR), the 5'-end of the core protein coding region, and the 3'- NCR. HCV genomic RNA contains an internal ribosome entry site (IRES) in the 5'-NCR which mediates translation independently of a 5'-cap structure (Wang *et al.*, 1993, *J. Virol.*, 67, 3338-44). The full-length sequence of the HCV RNA genome is heterologous among clinically isolated subtypes, of which there are at least 15 (Simmonds, 1995, *Hepatology*, 21, 570-583), however, the 5'-NCR sequence of HCV is highly conserved across all known subtypes, most likely to preserve the shared IRES mechanism (Okamoto *et al.*, 1991, *J. General Virol.*, 72, 2697-2704). In general, enzymatic nucleic acid molecules and nuclease activating compounds, and chimeras that cleave sites located in the 5' end of the HCV genome are expected to block translation while nucleic acid molecules and nuclease activating compounds, and chimeras that cleave sites located in the 3' end of the genome are expected to block RNA replication. Therefore, one nucleic acid molecule, compound, or chimera can be designed to cleave all the different isolates of HCV. Enzymatic nucleic acid molecules and nuclease activating compounds, and chimeras designed against conserved regions of various HCV isolates enable efficient inhibition of HCV replication in diverse patient populations and ensure the effectiveness of the nucleic acid molecules and nuclease activating compounds, and chimeras against HCV quasi species which evolve due to mutations in the non-conserved regions of the HCV genome.

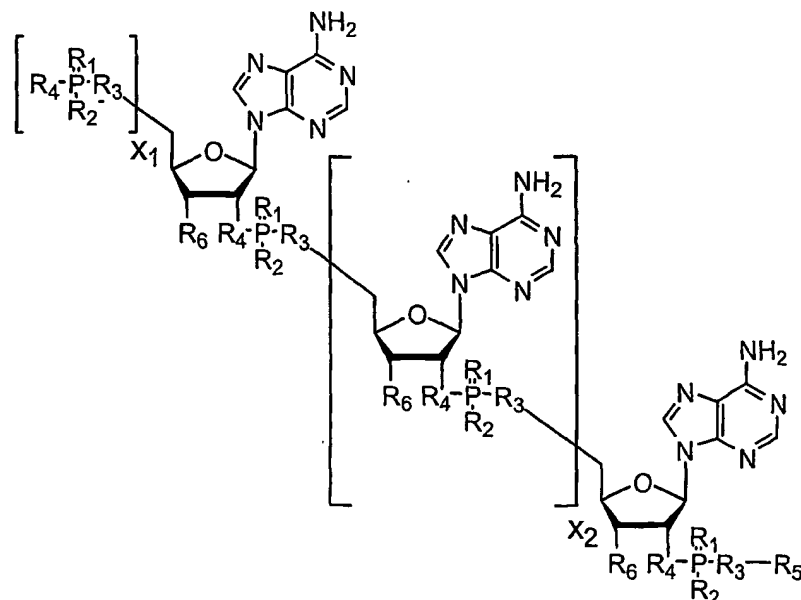
In one embodiment, the invention features an enzymatic nucleic acid molecule, preferably in the hammerhead, NCH (Inozyme), G-cleaver, amberzyme, zinzyme and/or DNAzyme motif, and the use thereof to down-regulate or inhibit the expression of HCV RNA.

In another embodiment, the invention features an enzymatic nucleic acid molecule, preferably in the hammerhead, Inozyme, G-cleaver, amberzyme, zinzyme and/or DNAzyme motif, and the use thereof to down-regulate or inhibit the expression of HCV minus strand RNA.

In yet another embodiment, the invention features a nuclease activating compound and/or a chimera and the use thereof to down-regulate or inhibit the expression of HCV RNA.

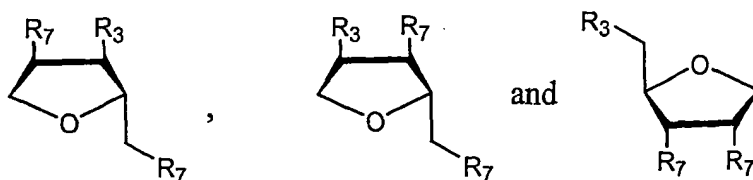
In another embodiment, the invention features the use of a nuclease activating compound and/or a chimera to inhibit the expression of HCV minus strand RNA.

In one embodiment, the invention features a compound having formula I:



wherein X_1 is an integer selected from the group consisting of 1, 2, and 3; X_2 is an integer greater than or equal to 1; R_6 is independently selected from the group including H, OH, NH_2 , O NH_2 , alkyl, S-alkyl, O-alkyl, O-alkyl-S-alkyl, O-alkoxyalkyl, allyl, O-allyl, and fluoro; each R_1 and R_2 are independently selected from the group consisting of O and S; each R_3 and R_4 are independently selected from the group consisting of O, N, and S; and R_5 is selected from the group consisting of alkyl, alkylamine, an oligonucleotide having any of SEQ ID NOS. 11343-16182, an oligonucleotide having a sequence complementary to a sequence selected from the group including SEQ ID NOS. 2594-7433, and abasic moiety.

In another embodiment, the abasic moiety of the instant invention is selected from the group consisting of:



wherein R_3 is selected from the group consisting of O, N, and S, and R_7 is independently selected from the group consisting of H, OH, NH_2 , O- NH_2 , alkyl, S-alkyl, O-alkyl, O-alkyl-S-alkyl, O-alkoxyalkyl, allyl, O-allyl, fluoro, oligonucleotide, alkyl, alkylamine and abasic moiety.

In another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid molecule.

In yet another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an antisense nucleic acid molecule.

In another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid molecule selected from the group consisting of Hammerhead, Inozyme, G-cleaver, DNAzyme, Amberzyme, and Zinzyme motifs.

In another embodiment, the Inozyme enzymatic nucleic acid molecule of the instant invention comprises a stem II region of length greater than or equal to 2 base pairs.

In one embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid comprising between 12 and 100 bases complementary to an RNA derived from HCV.

In another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid comprising between 14 and 24 bases complementary to said RNA derived from HCV.

In one embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an antisense nucleic acid comprising between 12 and 100 bases complementary to an RNA derived from HCV.

In another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an antisense nucleic acid comprising between 14 and 24 bases complementary to said RNA derived from HCV.

In another embodiment, the invention features a composition comprising a compound of Formula I, in a pharmaceutically acceptable carrier.

In yet another embodiment, the invention features a mammalian cell comprising a compound of Formula I. For example, the mammalian cell comprising a compound of Formula I can be a human cell.

In one embodiment, the invention features a method for the treatment of cirrhosis, liver failure, hepatocellular carcinoma, or a condition associated with HCV infection comprising

the step of administering to a patient a compound of Formula I under conditions suitable for said treatment.

In another embodiment, the invention features a method of treatment of a patient having a condition associated with HCV infection comprising contacting cells of said patient with a compound having Formula I, and further comprising the use of one or more drug therapies under conditions suitable for said treatment. For example, the other therapies of the instant invention can be selected from the group consisting of type I interferon, interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon, treatment with an enzymatic nucleic acid molecule, and treatment with an antisense molecule.

In another embodiment, the other therapies of the instant invention, for example type I interferon, interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon, treatment with an enzymatic nucleic acid molecule, and treatment with an antisense nucleic acid molecule, and the compound having Formula I are administered separately in separate pharmaceutically acceptable carriers.

In yet another embodiment, the other therapies of the instant invention, for example type I interferon, interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon, treatment with an enzymatic nucleic acid molecule, and treatment with an antisense nucleic acid molecule, and the compound having Formula I are administered simultaneously in a pharmaceutically acceptable carrier. The invention features a composition comprising a compound of Formula I and one or more of the above-listed compounds in a pharmaceutically acceptable carrier.

In yet another embodiment, the invention features a method for inhibiting HCV replication in a mammalian cell comprising the step of administering to said cell a compound having Formula I under conditions suitable for said inhibition.

In another embodiment, the invention features a method of cleaving a separate RNA molecule (i.e., HCV RNA or RNA necessary for HCV replication) comprising contacting a compound having Formula I with the separate RNA molecule under conditions suitable for the cleavage of the separate RNA molecule. In one example, the method of cleaving a separate RNA molecule is carried out in the presence of a divalent cation, for example Mg^{2+} .

In yet another embodiment, the method of cleaving a separate RNA molecule of the invention is carried out in the presence of a protein nuclease, for example RNase L.

In one embodiment, a compound having Formula I is chemically synthesized. In one embodiment, a compound having Formula I comprises at least one 2'-sugar modification, at least one nucleic acid base modification, and/or at least one phosphate modification.

The nucleic acid-based modulators of the invention are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells or tissues. The nucleic acid or nucleic acid complexes can be locally administered to relevant tissues *ex vivo*, or *in vivo* through injection, infusion pump or stent, with or without their incorporation in biopolymers. In particular embodiments, the nucleic acid molecules of the invention comprise sequences shown in **Tables IV-XI, XIV-XV and XVIII-XXIII**. Examples of such nucleic acid molecules consist essentially of sequences defined in the tables.

The nucleic acid-based inhibitors, nuclease activating compounds and chimeras of the invention are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells or tissues. The nucleic acid or nucleic acid complexes, and nuclease activating compounds or chimeras can be locally administered to relevant tissues *ex vivo*, or *in vivo* through injection or infusion pump, with or without their incorporation in biopolymers. In preferred embodiments, the enzymatic nucleic acid inhibitors, and nuclease activating compounds or chimeras comprise sequences, which are complementary to the substrate sequences in **Tables XVIII, XIX, XX and XXIII**. Examples of such enzymatic nucleic acid molecules also are shown in **Tables XVIII, XIX, XX, XXI and XXIII**. Examples of such enzymatic nucleic acid molecules consist essentially of sequences defined in these tables. In additional embodiments, the enzymatic nucleic acid inhibitors of the invention that comprise sequences which are complementary to the substrate sequences in **Tables XVIII, XIX, XX and XXIII** are covalently attached to nuclease activating compound or chimeras of the invention, for example a compound having Formula I.

In yet another embodiment, the invention features antisense nucleic acid molecules and 2-5A chimera including sequences complementary to the substrate sequences shown in **Tables XVIII, XIX, XX and XXIII**. Such nucleic acid molecules can include sequences as shown for the binding arms of the enzymatic nucleic acid molecules in **Tables XVIII, XIX, XX, XXI and XXIII**. Similarly, triplex molecules can be provided targeted to the corresponding DNA target regions, and containing the DNA equivalent of a target sequence or a sequence complementary to the specified target (substrate) sequence. Typically, antisense molecules are complementary to a target sequence along a single contiguous

sequence of the antisense molecule. However, in certain embodiments, an antisense molecule can bind to substrate such that the substrate molecule forms a loop, and/or an antisense molecule can bind such that the antisense molecule forms a loop. Thus, the antisense molecule can be complementary to two (or even more) non-contiguous substrate sequences or two (or even more) non-contiguous sequence portions of an antisense molecule can be complementary to a target sequence or both.

In one embodiment, the invention features nucleic acid molecules and nuclease activating compounds or chimeras that inhibit gene expression and/or viral replication. These chemically or enzymatically synthesized nucleic acid molecules can contain substrate binding domains that bind to accessible regions of their target mRNAs. The nucleic acid molecules also contain domains that catalyze the cleavage of RNA. The enzymatic nucleic acid molecules are preferably molecules of the hammerhead, Inozyme, DNAzyme, Zinzyme, Amberzyme, and/or G-cleaver motifs. Upon binding, the enzymatic nucleic acid molecules cleave the target mRNAs, preventing translation and protein accumulation. In the absence of the expression of the target gene, HCV gene expression and/or replication is inhibited.

In another aspect, the invention provides mammalian cells containing one or more nucleic acid molecules and/or expression vectors of this invention. The one or more nucleic acid molecules can independently be targeted to the same or different sites.

In one embodiment, nucleic acid decoys, aptamers, siRNA, enzymatic nucleic acids or antisense molecules that interact with target protein and/or RNA molecules and modulate HBV (specifically HBV reverse transcriptase, or transcription of HBV genomic DNA) activity are expressed from transcription units inserted into DNA or RNA vectors. The recombinant vectors are preferably DNA plasmids or viral vectors. Decoys, aptamers, enzymatic nucleic acid or antisense expressing viral vectors can be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, the recombinant vectors capable of expressing the decoys, aptamers, enzymatic nucleic acids or antisense are delivered as described above, and persist in target cells. Alternatively, viral vectors can be used that provide for transient expression of decoys, aptamers, siRNA, enzymatic nucleic acids or antisense. Such vectors can be repeatedly administered as necessary. Once expressed, the decoys, aptamers, enzymatic nucleic acids or antisense bind to the target protein and/or RNA and modulate its function or expression. Delivery of decoy, aptamer, siRNA, enzymatic nucleic acid or antisense expressing vectors can be systemic, such as by intravenous or intramuscular administration, by administration to target cells explanted from the patient followed by reintroduction into the patient, or by any other means that would allow for introduction into the desired target cell. DNA based nucleic acid

molecules of the invention can be expressed via the use of a single stranded DNA intracellular expression vector.

In one embodiment, nucleic acid molecules and nuclease activating compounds or chimeras are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells. The nucleic acid or nucleic acid complexes can be locally administered to relevant tissues *ex vivo*, or *in vivo* through injection, infusion pump or stent, with or without their incorporation in biopolymers. In another preferred embodiment, the nucleic acid molecule, nuclease activating compound or chimera is administered to the site of HBV or HCV activity (e.g., hepatocytes) in an appropriate liposomal vehicle.

In another embodiment, nucleic acid molecules that cleave target molecules and inhibit HCV activity are expressed from transcription units inserted into DNA or RNA vectors. The recombinant vectors are preferably DNA plasmids or viral vectors. Nucleic acid molecule expressing viral vectors can be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, the recombinant vectors capable of expressing the nucleic acid molecules are delivered as described above, and persist in target cells. Alternatively, viral vectors can be used that provide for transient expression of nucleic acid molecules. Such vectors can be repeatedly administered as necessary. Once expressed, the nucleic acid molecules cleave the target mRNA. Delivery of enzymatic nucleic acid molecule expressing vectors can be systemic, such as by intravenous or intramuscular administration, by administration to target cells *ex-planted* from the patient followed by reintroduction into the patient, or by any other means that would allow for introduction into the desired target cell (for a review see Couture and Stinchcomb, 1996, *TIG.*, 12, 510). In another aspect of the invention, nucleic acid molecules that cleave target molecules and inhibit viral replication are expressed from transcription units inserted into DNA, RNA, or viral vectors. Preferably, the recombinant vectors capable of expressing the nucleic acid molecules are locally delivered as described above, and transiently persist in smooth muscle cells. However, other mammalian cell vectors that direct the expression of RNA can be used for this purpose.

The nucleic acid molecules of the instant invention, individually, or in combination or in conjunction with other drugs, and/or therapies can be used to treat diseases or conditions discussed herein. For example, to treat a disease or condition associated with the levels of HBV or HCV, the nucleic acid molecules can be administered to a patient or can be administered to other appropriate cells evident to those skilled in the art, individually or in combination with one or more drugs under conditions suitable for the treatment.

In a further embodiment, the described molecules, such as decoys, aptamers, antisense, enzymatic nucleic acids, or nuclease activating compounds and chimeras can be used in combination with other known treatments to treat conditions or diseases discussed above. For example, the described molecules could be used in combination with one or more known therapeutic agents to treat HBV infection, HCV infection, hepatitis, hepatocellular carcinoma, cancer, cirrhosis, and liver failure. Such therapeutic agents can include, but are not limited to, nucleoside analogs selected from the group comprising Lamivudine (3TC®), L-FMAU, and/or adefovir dipivoxil (for a review of applicable nucleoside analogs, see Colacino and Staschke, 1998, *Progress in Drug Research*, 50, 259-322). Immunomodulators selected from the group comprising Type 1 Interferon, therapeutic vaccines, steroids, and 2'-5' oligoadenylates (for a review of 2'-5' Oligoadenylates, see Charubala and Pfeleiderer, 1994, *Progress in Molecular and Subcellular Biology*, 14, 113-138).

Nucleic acid molecules, nuclease activating compounds and chimeras of the invention, individually, or in combination or in conjunction with other drugs, can be used to treat diseases or conditions discussed above. For example, to treat a disease or condition associated with HBV or HCV levels, the patient can be treated, or other appropriate cells can be treated, as is evident to those skilled in the art.

In a further embodiment, the described molecules can be used in combination with other known treatments to treat conditions or diseases discussed above. For example, the described molecules can be used in combination with one or more known therapeutic agents to treat liver failure, hepatocellular carcinoma, cirrhosis, and/or other disease states associated with HBV or HCV infection. Additional known therapeutic agents are those comprising antivirals, interferons, and/or antisense compounds.

The term "inhibit" or "down-regulate" as used herein refers to the expression of the gene, or level of RNAs or equivalent RNAs encoding one or more protein subunits or components, or activity of one or more protein subunits or components, such as HBV protein or proteins, is reduced below that observed in the absence of the therapies of the invention. In one embodiment, inhibition or down-regulation with enzymatic nucleic acid molecule preferably is below that level observed in the presence of an enzymatically inactive or attenuated molecule that is able to bind to the same site on the target RNA, but is unable to cleave that RNA. In another embodiment, inhibition or down-regulation with antisense oligonucleotides is preferably below that level observed in the presence of, for example, an oligonucleotide with scrambled sequence or with mismatches. In another embodiment, inhibition or down-regulation of HBV with the nucleic acid molecule of the instant invention is greater in the presence of the nucleic acid molecule than in its absence.

The term "up-regulate" as used herein refers to the expression of the gene, or level of RNAs or equivalent RNAs encoding one or more protein subunits or components, or activity of one or more protein subunits or components, such as HBV or HCV protein or proteins, is greater than that observed in the absence of the therapies of the invention. For example, the expression of a gene, such as HBV or HCV genes, can be increased in order to treat, prevent, ameliorate, or modulate a pathological condition caused or exacerbated by an absence or low level of gene expression.

The term "modulate" as used herein refers to the expression of the gene, or level of RNAs or equivalent RNAs encoding one or more protein subunits or components, or activity of one or more proteins is up-regulated or down-regulated, such that the expression, level, or activity is greater than or less than that observed in the absence of the therapies of the invention.

The term "decoy" as used herein refers to a nucleic acid molecule, for example RNA or DNA, or aptamer that is designed to preferentially bind to a predetermined ligand. Such binding can result in the inhibition or activation of a target molecule. A decoy or aptamer can compete with a naturally occurring binding target for the binding of a specific ligand. For example, it has been shown that over-expression of HIV trans-activation response (TAR) RNA can act as a "decoy" and efficiently binds HIV tat protein, thereby preventing it from binding to TAR sequences encoded in the HIV RNA (Sullenger *et al.*, 1990, *Cell*, 63, 601-608). This is but a specific example and those in the art will recognize that other embodiments can be readily generated using techniques generally known in the art, see for example Gold *et al.*, 1995, *Annu. Rev. Biochem.*, 64, 763; Brody and Gold, 2000, *J. Biotechnol.*, 74, 5; Sun, 2000, *Curr. Opin. Mol. Ther.*, 2, 100; Kusser, 2000, *J. Biotechnol.*, 74, 27; Hermann and Patel, 2000, *Science*, 287, 820; and Jayasena, 1999, *Clinical Chemistry*, 45, 1628. Similarly, a decoy can be designed to bind to HBV or HCV proteins and block the binding of HBV or HCV DNA or RNA or a decoy can be designed to bind to HBV or HCV proteins and prevent molecular interaction with the HBV or HCV proteins.

By "aptamer" or "nucleic acid aptamer" as used herein is meant a nucleic acid molecule that binds specifically to a target molecule wherein the nucleic acid molecule has sequence that is distinct from sequence recognized by the target molecule in its natural setting. Alternately, an aptamer can be a nucleic acid molecule that binds to a target molecule where the target molecule does not naturally bind to a nucleic acid. The target molecule can be any molecule of interest. For example, the aptamer can be used to bind to a ligand-binding domain of a protein, thereby preventing interaction of the naturally occurring ligand with the protein. This is a non-limiting example and those in the art will recognize that other embodiments can be readily generated using techniques generally known in the art, see for

example Gold *et al.*, 1995, *Annu. Rev. Biochem.*, 64, 763; Brody and Gold, 2000, *J. Biotechnol.*, 74, 5; Sun, 2000, *Curr. Opin. Mol. Ther.*, 2, 100; Kusser, 2000, *J. Biotechnol.*, 74, 27; Hermann and Patel, 2000, *Science*, 287, 820; and Jayasena, 1999, *Clinical Chemistry*, 45, 1628.

By "enzymatic nucleic acid molecule" is meant a nucleic acid molecule that has complementarity in a substrate binding region to a specified gene target, and also has an enzymatic activity which is active to specifically cleave a target RNA molecule. That is, the enzymatic nucleic acid molecule is able to intermolecularly cleave a RNA molecule and thereby inactivate a target RNA molecule. These complementary regions allow sufficient hybridization of the enzymatic nucleic acid molecule to a target RNA molecule and thus permit cleavage. One hundred percent complementarity is preferred, but complementarity as low as 50-75% may also be useful in this invention (see for example Werner and Uhlenbeck, 1995, *Nucleic Acids Research*, 23, 2092-2096; Hammann *et al.*, 1999, *Antisense and Nucleic Acid Drug Dev.*, 9, 25-31). The nucleic acids can be modified at the base, sugar, and/or phosphate groups. The term enzymatic nucleic acid is used interchangeably with phrases such as ribozymes, catalytic RNA, enzymatic RNA, catalytic DNA, aptazyme or aptamer-binding ribozyme, regulatable ribozyme, catalytic oligonucleotides, nucleozyme, DNAzyme, RNA enzyme, endoribonuclease, endonuclease, minizyme, leadzyme, oligozyme or DNA enzyme. All of these terminologies describe nucleic acid molecules with enzymatic activity. The specific enzymatic nucleic acid molecules described in the instant application are not limiting in the invention and those skilled in the art will recognize that all that is important in an enzymatic nucleic acid molecule of this invention is that it have a specific substrate binding site which is complementary to one or more of the target nucleic acid regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart a nucleic acid cleaving activity to the molecule (Cech *et al.*, U.S. Patent No. 4,987,071; Cech *et al.*, 1988, *JAMA* 260:20 3030-4).

By "nucleic acid molecule" as used herein is meant a molecule comprising nucleotides. The nucleic acid can be single, double, or multiple stranded and can comprise modified or unmodified nucleotides or non-nucleotides or various mixtures and combinations thereof.

By "enzymatic portion" or "catalytic domain" is meant that portion/region of the enzymatic nucleic acid molecule essential for cleavage of a nucleic acid substrate (for example see **Figures 1-5**).

By "substrate binding arm" or "substrate binding domain" is meant that portion/region of a ribozyme which is complementary to (*i.e.*, able to base-pair with) a portion of its substrate. Generally, such complementarity is 100%, but can be less if desired. For example, as few as 10 bases out of 14 may be base-paired (see for example Werner and Uhlenbeck,

1995, *Nucleic Acids Research*, 23, 2092-2096; Hammann *et al.*, 1999, *Antisense and Nucleic Acid Drug Dev.*, 9, 25-31). Such arms are shown generally in **Figures 1-5**. That is, these arms contain sequences within a ribozyme which are intended to bring ribozyme and target RNA together through complementary base-pairing interactions. The ribozyme of the invention can have binding arms that are contiguous or non-contiguous and may be of varying lengths. The length of the binding arm(s) are preferably greater than or equal to four nucleotides and of sufficient length to stably interact with the target RNA; specifically 12-100 nucleotides; more specifically 14-24 nucleotides long (see for example Werner and Uhlenbeck, *supra*; Hamman *et al.*, *supra*; Hampel *et al.*, EP0360257; Berzal-Herrance *et al.*, 1993, *EMBO J.*, 12, 2567-73). If two binding arms are chosen, the design is such that the length of the binding arms are symmetrical (*i.e.*, each of the binding arms is of the same length; *e.g.*, five and five nucleotides, six and six nucleotides or seven and seven nucleotides long) or asymmetrical (*i.e.*, the binding arms are of different length; *e.g.*, six and three nucleotides; three and six nucleotides long; four and five nucleotides long; four and six nucleotides long; four and seven nucleotides long; and the like).

By "nuclease activating compound" is meant a compound, for example a compound having Formula I, that activates the cleavage of an RNA by a nuclease. The nuclease can comprise RNase L. By "nuclease activating chimera" or "chimera" is meant a nuclease activating compound, for example a compound having Formula I, that is attached to a nucleic acid molecule, for example a nucleic acid molecule that binds preferentially to a target RNA. These chimeric nucleic acid molecules can comprise a nuclease activating compound and an antisense nucleic acid molecule, for example a 2',5'-oligoadenylate antisense chimera, or an enzymatic nucleic acid molecule, for example a 2',5'-oligoadenylate enzymatic nucleic acid chimera.

By "Inozyme" or "NCH" motif or configuration is meant, an enzymatic nucleic acid molecule comprising a motif as is generally described as NCH Rz in Ludwig *et al.*, International PCT Publication No. WO 98/58058 and US Patent Application Serial No. 08/878,640. Inozymes possess endonuclease activity to cleave RNA substrates having a cleavage triplet NCH/, where N is a nucleotide, C is cytidine and H is adenosine, uridine or cytidine, and / represents the cleavage site. Inozymes can also possess endonuclease activity to cleave RNA substrates having a cleavage triplet NCN/, where N is a nucleotide, C is cytidine, and / represents the cleavage site.

By "G-cleaver" motif or configuration is meant, an enzymatic nucleic acid molecule comprising a motif as is generally described in Eckstein *et al.*, US 6,127,173 and in Kore *et al.*, 1998, *Nucleic Acids Research* 26, 4116-4120. G-cleavers possess endonuclease activity

to cleave RNA substrates having a cleavage triplet NYN/, where N is a nucleotide, Y is uridine or cytidine and / represents the cleavage site. G-cleavers can be chemically modified.

By "zinzyme" motif or configuration is meant, an enzymatic nucleic acid molecule comprising a motif as is generally described in Beigelman *et al.*, International PCT publication No. WO 99/55857 and US Patent Application Serial No. 09/918,728. Zinzymes possess endonuclease activity to cleave RNA substrates having a cleavage triplet including but not limited to, YG/Y, where Y is uridine or cytidine, and G is guanosine and / represents the cleavage site. Zinzymes can be chemically modified to increase nuclease stability through various substitutions, including substituting 2'-O-methyl guanosine nucleotides for guanosine nucleotides. In addition, differing nucleotide and/or non-nucleotide linkers can be used to substitute the 5'-gaaa-2' loop of the motif. Zinzymes represent a non-limiting example of an enzymatic nucleic acid molecule that does not require a ribonucleotide (2'-OH) group within its own nucleic acid sequence for activity.

By "amberzyme" motif or configuration is meant, an enzymatic nucleic acid molecule comprising a motif as is generally described in Beigelman *et al.*, International PCT publication No. WO 99/55857 and US Patent Application Serial No. 09/476,387. Amberzymes possess endonuclease activity to cleave RNA substrates having a cleavage triplet NG/N, where N is a nucleotide, G is guanosine, and / represents the cleavage site. Amberzymes can be chemically modified to increase nuclease stability. In addition, differing nucleoside and/or non-nucleoside linkers can be used to substitute the 5'-gaaa-3' loops of the motif. Amberzymes represent a non-limiting example of an enzymatic nucleic acid molecule that does not require a ribonucleotide (2'-OH) group within its own nucleic acid sequence for activity.

By 'DNAzyme' is meant, an enzymatic nucleic acid molecule that does not require the presence of a 2'-OH group within its own nucleic acid sequence for activity. In particular embodiments, the enzymatic nucleic acid molecule can have an attached linker or linkers or other attached or associated groups, moieties, or chains containing one or more nucleotides with 2'-OH groups. DNAzymes can be synthesized chemically or expressed endogenously *in vivo*, by means of a single stranded DNA vector or equivalent thereof. Non-limiting examples of DNAzymes are generally reviewed in Usman *et al.*, US patent No., 6,159,714; Chartrand *et al.*, 1995, *NAR* 23, 4092; Breaker *et al.*, 1995, *Chem. Bio.* 2, 655; Santoro *et al.*, 1997, *PNAS* 94, 4262; Breaker, 1999, *Nature Biotechnology*, 17, 422-423; and Santoro *et al.*, 2000, *J. Am. Chem. Soc.*, 122, 2433-39. The "10-23" DNAzyme motif is one particular type of DNAzyme that was evolved using *in vitro* selection as generally described in Joyce *et al.*, US 5,807,718 and Santoro *et al.*, *supra*. Additional DNAzyme motifs can be selected for

using techniques similar to those described in these references, and hence, are within the scope of the present invention.

By “nucleic acid sensor molecule” or “allozyme” as used herein is meant a nucleic acid molecule comprising an enzymatic domain and a sensor domain, where the enzymatic nucleic acid domain’s ability to catalyze a chemical reaction is dependent on the interaction with a target signaling molecule, such as a nucleic acid, polynucleotide, oligonucleotide, peptide, polypeptide, or protein, for example HBV RT, HBV RT primer, or HBV Enhancer I sequence. The introduction of chemical modifications, additional functional groups, and/or linkers, to the nucleic acid sensor molecule can provide enhanced catalytic activity of the nucleic acid sensor molecule, increased binding affinity of the sensor domain to a target nucleic acid, and/or improved nuclease/chemical stability of the nucleic acid sensor molecule, and are hence within the scope of the present invention (see for example Usman *et al.*, US Patent Application No. 09/877,526, George *et al.*, US Patent Nos. 5,834,186 and 5,741,679, Shih *et al.*, US Patent No. 5,589,332, Nathan *et al.*, US Patent No 5,871,914, Nathan and Ellington, International PCT publication No. WO 00/24931, Breaker *et al.*, International PCT Publication Nos. WO 00/26226 and 98/27104, and Sullenger *et al.*, US Patent Application Serial No. 09/205,520).

By “sensor component” or “sensor domain” of the nucleic acid sensor molecule as used herein is meant, a nucleic acid sequence (e.g., RNA or DNA or analogs thereof) which interacts with a target signaling molecule, for example a nucleic acid sequence in one or more regions of a target nucleic acid molecule or more than one target nucleic acid molecule, and which interaction causes the enzymatic nucleic acid component of the nucleic acid sensor molecule to either catalyze a reaction or stop catalyzing a reaction. In the presence of target signaling molecule of the invention, such as HBV RT, HBV RT primer, or HBV Enhancer I sequence, the ability of the sensor component, for example, to modulate the catalytic activity of the nucleic acid sensor molecule, is altered or diminished in a manner that can be detected or measured. The sensor component can comprise recognition properties relating to chemical or physical signals capable of modulating the nucleic acid sensor molecule via chemical or physical changes to the structure of the nucleic acid sensor molecule. The sensor component can be derived from a naturally occurring nucleic acid binding sequence, for example, RNAs that bind to other nucleic acid sequences *in vivo*. Alternately, the sensor component can be derived from a nucleic acid molecule (aptamer), which is evolved to bind to a nucleic acid sequence within a target nucleic acid molecule. The sensor component can be covalently linked to the nucleic acid sensor molecule, or can be non-covalently associated. A person skilled in the art will recognize that all that is required is that the sensor component is able to selectively modulate the activity of the nucleic acid sensor molecule to catalyze a reaction.

By "target molecule" or "target signaling molecule" is meant a molecule capable of interacting with a nucleic acid sensor molecule, specifically a sensor domain of a nucleic acid sensor molecule, in a manner that causes the nucleic acid sensor molecule to be active or inactive. The interaction of the signaling agent with a nucleic acid sensor molecule can result in modification of the enzymatic nucleic acid component of the nucleic acid sensor molecule via chemical, physical, topological, or conformational changes to the structure of the molecule, such that the activity of the enzymatic nucleic acid component of the nucleic acid sensor molecule is modulated, for example is activated or inactivated. Signaling agents can comprise target signaling molecules such as macromolecules, ligands, small molecules, metals and ions, nucleic acid molecules including but not limited to RNA and DNA or analogs thereof, proteins, peptides, antibodies, polysaccharides, lipids, sugars, microbial or cellular metabolites, pharmaceuticals, and organic and inorganic molecules in a purified or unpurified form, for example HBV RT or HBV RT primer.

By "sufficient length" is meant a nucleic acid molecule long enough to provide the intended function under the expected condition. For example, a nucleic acid molecule of the invention needs to be of "sufficient length" to provide stable binding to a target site under the expected binding conditions and environment. In another non-limiting example, for the binding arms of an enzymatic nucleic acid, "sufficient length" means that the binding arm sequence is long enough to provide stable binding to a target site under the expected reaction conditions and environment. The binding arms are not so long as to prevent useful turnover of the nucleic acid molecule. By "stably interact" is meant interaction of the oligonucleotides with target nucleic acid (*e.g.*, by forming hydrogen bonds with complementary nucleotides in the target under physiological conditions) that is sufficient for the intended purpose (*e.g.*, cleavage of target RNA by an enzyme).

By "equivalent" RNA to HBV or HCV is meant to include those naturally occurring RNA molecules having homology (partial or complete) to HBV or HCV proteins or encoding for proteins with similar function as HBV or HCV in various organisms, including human, rodent, primate, rabbit, pig, protozoans, fungi, plants, and other microorganisms and parasites. The equivalent RNA sequence also includes in addition to the coding region, regions such as 5'-untranslated region, 3'-untranslated region, introns, intron-exon junction and the like.

The term "component" of HBV or HCV as used herein refers to a peptide or protein subunit expressed from a HBV or HCV gene.

By "homology" is meant the nucleotide sequence of two or more nucleic acid molecules is partially or completely identical.

By "antisense nucleic acid", it is meant a non-enzymatic nucleic acid molecule that binds to target RNA by means of RNA-RNA or RNA-DNA or RNA-PNA (protein nucleic acid; Egholm *et al.*, 1993 *Nature* 365, 566) interactions and alters the activity of the target RNA (for a review, see Stein and Cheng, 1993 *Science* 261, 1004 and Woolf *et al.*, US patent No. 5,849,902). Typically, antisense molecules are complementary to a target sequence along a single contiguous sequence of the antisense molecule. However, in certain embodiments, an antisense molecule can bind to substrate such that the substrate molecule forms a loop, and/or an antisense molecule can bind such that the antisense molecule forms a loop. Thus, the antisense molecule can be complementary to two or more non-contiguous substrate sequences or two or more non-contiguous sequence portions of an antisense molecule can be complementary to a target sequence, or both. For a review of current antisense strategies, see Schmajuk *et al.*, 1999, *J. Biol. Chem.*, 274, 21783-21789, Delihias *et al.*, 1997, *Nature*, 15, 751-753, Stein *et al.*, 1997, *Antisense N. A. Drug Dev.*, 7, 151, Crooke, 2000, *Methods Enzymol.*, 313, 3-45; Crooke, 1998, *Biotech. Genet. Eng. Rev.*, 15, 121-157, Crooke, 1997, *Ad. Pharmacol.*, 40, 1-49. Antisense molecules of the instant invention can include 2-5A antisense chimera molecules. In addition, antisense DNA can be used to target RNA by means of DNA-RNA interactions, thereby activating RNase H, which digests the target RNA in the duplex. The antisense oligonucleotides can comprise one or more RNase H activating region that is capable of activating RNase H cleavage of a target RNA. Antisense DNA can be synthesized chemically or expressed via the use of a single stranded DNA expression vector or equivalent thereof.

By "RNase H activating region" is meant a region (generally greater than or equal to 4-25 nucleotides in length, preferably from 5-11 nucleotides in length) of a nucleic acid molecule capable of binding to a target RNA to form a non-covalent complex that is recognized by cellular RNase H enzyme (see for example Arrow *et al.*, US 5,849,902; Arrow *et al.*, US 5,989,912). The RNase H enzyme binds to the nucleic acid molecule-target RNA complex and cleaves the target RNA sequence. The RNase H activating region comprises, for example, phosphodiester, phosphorothioate (for example, at least four of the nucleotides are phosphorothioate substitutions; more specifically, 4-11 of the nucleotides are phosphorothioate substitutions), phosphorodithioate, 5'-thiophosphate, or methylphosphonate backbone chemistry or a combination thereof. In addition to one or more backbone chemistries described above, the RNase H activating region can also comprise a variety of sugar chemistries. For example, the RNase H activating region can comprise deoxyribose, arabino, fluoroarabino or a combination thereof, nucleotide sugar chemistry. Those skilled in the art will recognize that the foregoing are non-limiting examples and that any combination

of phosphate, sugar and base chemistry of a nucleic acid that supports the activity of RNase H enzyme is within the scope of the definition of the RNase H activating region and the instant invention.

By "2-5A antisense" or "2-5A antisense chimera" is meant an antisense oligonucleotide containing a 5'-phosphorylated 2'-5'-linked adenylyate residue. These chimeras bind to target RNA in a sequence-specific manner and activate a cellular 2-5A-dependent ribonuclease which, in turn, cleaves the target RNA (Torrence *et al.*, 1993 *Proc. Natl. Acad. Sci. USA* 90, 1300; Silverman *et al.*, 2000, *Methods Enzymol.*, 313, 522-533; Player and Torrence, 1998, *Pharmacol. Ther.*, 78, 55-113).

By "triplex nucleic acid" or "triplex oligonucleotide" it is meant a polynucleotide or oligonucleotide that can bind to a double-stranded DNA in a sequence-specific manner to form a triple-strand helix. Formation of such triple helix structure has been shown to modulate transcription of the targeted gene (Duval-Valentin *et al.*, 1992, *Proc. Natl. Acad. Sci. USA*, 89, 504). Triplex nucleic acid molecules of the invention also include steric blocker nucleic acid molecules that bind to the Enhancer I region of HBV DNA (plus strand and/or minus strand) and prevent translation of HBV genomic DNA.

The term "single stranded RNA" (ssRNA) as used herein refers to a naturally occurring or synthetic ribonucleic acid molecule comprising a linear single strand, for example a ssRNA can be a messenger RNA (mRNA), transfer RNA (tRNA), ribosomal RNA (rRNA) etc. of a gene.

The term "single stranded DNA" (ssDNA) as used herein refers to a naturally occurring or synthetic deoxyribonucleic acid molecule comprising a linear single strand, for example, a ssDNA can be a sense or antisense gene sequence or EST (Expressed Sequence Tag).

The term "allozyme" as used herein refers to an allosteric enzymatic nucleic acid molecule, see for example George *et al.*, US Patent Nos. 5,834,186 and 5,741,679, Shih *et al.*, US Patent No. 5,589,332, Nathan *et al.*, US Patent No 5,871,914, Nathan and Ellington, International PCT publication No. WO 00/24931, Breaker *et al.*, International PCT Publication Nos. WO 00/26226 and 98/27104, and Sullenger *et al.*, International PCT publication No. WO 99/29842.

The term "2-5A chimera" as used herein refers to an oligonucleotide containing a 5'-phosphorylated 2'-5'-linked adenylyate residue. These chimeras bind to target RNA in a sequence-specific manner and activate a cellular 2-5A-dependent ribonuclease which, in turn, cleaves the target RNA (Torrence *et al.*, 1993 *Proc. Natl. Acad. Sci. USA* 90, 1300;

Silverman *et al.*, 2000, *Methods Enzymol.*, 313, 522-533; Player and Torrence, 1998, *Pharmacol. Ther.*, 78, 55-113).

The term "double stranded RNA" or "dsRNA" as used herein refers to a double stranded RNA molecule capable of RNA interference "RNAi", including short interfering RNA "siRNA" see for example Bass, 2001, *Nature*, 411, 428-429; Elbashir *et al.*, 2001, *Nature*, 411, 494-498; and Kreutzer *et al.*, International PCT Publication No. WO 00/44895; Zernicka-Goetz *et al.*, International PCT Publication No. WO 01/36646; Fire, International PCT Publication No. WO 99/32619; Plaetinck *et al.*, International PCT Publication No. WO 00/01846; Mello and Fire, International PCT Publication No. WO 01/29058; Deschamps-Depaillette, International PCT Publication No. WO 99/07409; and Li *et al.*, International PCT Publication No. WO 00/44914.

By "gene" it is meant, a nucleic acid that encodes an RNA, for example, nucleic acid sequences including, but not limited to, structural genes encoding a polypeptide.

By "complementarity" is meant that a nucleic acid can form hydrogen bond(s) with another nucleic acid sequence by either traditional Watson-Crick or other non-traditional types. In reference to the nucleic molecules of the present invention, the binding free energy for a nucleic acid molecule with its target or complementary sequence is sufficient to allow the relevant function of the nucleic acid to proceed, e.g., ribozyme cleavage, antisense or triple helix modulation. Determination of binding free energies for nucleic acid molecules is well known in the art (see, e.g., Turner *et al.*, 1987, *CSH Symp. Quant. Biol.* LII pp.123-133; Frier *et al.*, 1986, *Proc. Nat. Acad. Sci. USA* 83:9373-9377; Turner *et al.*, 1987, *J. Am. Chem. Soc.* 109:3783-3785). A percent complementarity indicates the percentage of contiguous residues in a nucleic acid molecule that can form hydrogen bonds (e.g., Watson-Crick base pairing) with a second nucleic acid sequence (e.g., 5, 6, 7, 8, 9, 10 out of 10 being 50%, 60%, 70%, 80%, 90%, and 100% complementary). "Perfectly complementary" means that all the contiguous residues of a nucleic acid sequence will hydrogen bond with the same number of contiguous residues in a second nucleic acid sequence.

As used herein "cell" is used in its usual biological sense, and does not refer to an entire multicellular organism, e.g., specifically does not refer to a human. The cell can be present in an organism, e.g., birds, plants and mammals such as humans, cows, sheep, apes, monkeys, swine, dogs, and cats. The cell can be prokaryotic (e.g., bacterial cell) or eukaryotic (e.g., mammalian or plant cell).

By "HBV proteins" or "HCV proteins" is meant, a protein or a mutant protein derivative thereof, comprising sequence expressed and/or encoded by the HBV genome.

By "highly conserved sequence region" is meant a nucleotide sequence of one or more regions in a target gene does not vary significantly from one generation to the other or from one biological system to the other.

By "highly conserved nucleic acid binding region" is meant an amino acid sequence of one or more regions in a target protein that does not vary significantly from one generation to the other or from one biological system to the other.

By "related to the levels of HBV" is meant that the reduction of HBV expression (specifically HBV gene) RNA levels and thus reduction in the level of the respective protein will relieve, to some extent, the symptoms of the disease or condition.

By "related to the levels of HCV" is meant that the reduction of HCV expression (specifically HCV gene) RNA levels and thus reduction in the level of the respective protein will relieve, to some extent, the symptoms of the disease or condition.

By "RNA" is meant a molecule comprising at least one ribonucleotide residue. By "ribonucleotide" is meant a nucleotide with a hydroxyl group at the 2' position of a β -D-ribofuranose moiety.

By "vector" is meant any nucleic acid- and/or viral-based technique used to express and/or deliver a desired nucleic acid.

By "patient" is meant an organism, which is a donor or recipient of explanted cells or the cells themselves. "Patient" also refers to an organism to which the nucleic acid molecules of the invention can be administered. In one embodiment, a patient is a mammal or mammalian cells. In another embodiment, a patient is a human or human cells.

Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof, and from the claims.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

First the drawings will be described briefly.

Drawings

Figure 1 shows the secondary structure model for seven different classes of enzymatic nucleic acid molecules. Arrow indicates the site of cleavage. ----- indicate the target sequence. Lines interspersed with dots are meant to indicate tertiary interactions. - is meant to

indicate base-paired interaction. **Group I Intron:** P1-P9.0 represent various stem-loop structures (Cech *et al.*, 1994, *Nature Struct. Bio.*, 1, 273). **RNase P (MIRNA):** EGS represents external guide sequence (Forster *et al.*, 1990, *Science*, 249, 783; Pace *et al.*, 1990, *J. Biol. Chem.*, 265, 3587). **Group II Intron:** 5'SS means 5' splice site; 3'SS means 3'-splice site; IBS means intron binding site; EBS means exon binding site (Pyle *et al.*, 1994, *Biochemistry*, 33, 2716). **VS RNA:** I-VI are meant to indicate six stem-loop structures; shaded regions are meant to indicate tertiary interaction (Collins, International PCT Publication No. WO 96/19577). **HDV Ribozyme:** I-IV are meant to indicate four stem-loop structures (Been *et al.*, US Patent No. 5,625,047). **Hammerhead Ribozyme:** I-III are meant to indicate three stem-loop structures; stems I-III can be of any length and may be symmetrical or asymmetrical (Usman *et al.*, 1996, *Curr. Op. Struct. Bio.*, 1, 527). **Hairpin Ribozyme:** Helix 1, 4 and 5 can be of any length; Helix 2 is between 3 and 8 base-pairs long; Y is a pyrimidine; Helix 2 (H2) is provided with a least 4 base pairs (*i.e.*, n is 1, 2, 3 or 4) and helix 5 can be optionally provided of length 2 or more bases (preferably 3 - 20 bases, *i.e.*, m is from 1 - 20 or more). Helix 2 and helix 5 may be covalently linked by one or more bases (*i.e.*, r is ≥ 1 base). Helix 1, 4 or 5 may also be extended by 2 or more base pairs (*e.g.*, 4 - 20 base pairs) to stabilize the ribozyme structure, and preferably is a protein binding site. In each instance, each N and N' independently is any normal or modified base and each dash represents a potential base-pairing interaction. These nucleotides may be modified at the sugar, base or phosphate. Complete base-pairing is not required in the helices, but is preferred. Helix 1 and 4 can be of any size (*i.e.*, o and p is each independently from 0 to any number, *e.g.*, 20) as long as some base-pairing is maintained. Essential bases are shown as specific bases in the structure, but those in the art will recognize that one or more may be modified chemically (abasic, base, sugar and/or phosphate modifications) or replaced with another base without significant effect. Helix 4 can be formed from two separate molecules, *i.e.*, without a connecting loop. The connecting loop when present may be a ribonucleotide with or without modifications to its base, sugar or phosphate. "q" ≥ 2 bases. The connecting loop can also be replaced with a non-nucleotide linker molecule. H refers to bases A, U, or C. Y refers to pyrimidine bases. "_____" refers to a covalent bond. (Burke *et al.*, 1996, *Nucleic Acids & Mol. Biol.*, 10, 129; Chowrira *et al.*, US Patent No. 5,631,359).

Figure 2 shows examples of chemically stabilized ribozyme motifs. **HH Rz**, represents hammerhead ribozyme motif (Usman *et al.*, 1996, *Curr. Op. Struct. Bio.*, 1, 527); **NCH Rz** represents the NCH ribozyme motif (Ludwig & Sproat, International PCT Publication No. WO 98/58058); **G-Cleaver**, represents G-cleaver ribozyme motif (Kore *et al.*, 1998, *Nucleic Acids Research*, 26, 4116-4120). N or n, represent independently a nucleotide which may be same or different and have complementarity to each other; **rI**, represents ribo-Inosine nucleotide; arrow indicates the site of cleavage within the target. Position 4 of the HH Rz and the NCH Rz is shown as having 2'-C-allyl modification, but

those skilled in the art will recognize that this position can be modified with other modifications well known in the art, so long as such modifications do not significantly inhibit the activity of the ribozyme.

Figure 3 shows an example of the Amberzyme ribozyme motif that is chemically stabilized (see, for example, Beigelman *et al.*, International PCT publication No. WO 99/55857; also referred to as Class I Motif). The Amberzyme motif is a class of enzymatic nucleic acid molecules that do not require the presence of a ribonucleotide (2'-OH) group for activity.

Figure 4 shows an example of the Zinzyme A ribozyme motif that is chemically stabilized (see, for example, International PCT publication No. WO 99/55857; also referred to as Class A Motif). The Zinzyme motif is a class of enzymatic nucleic acid molecules that do not require the presence of a ribonucleotide (2'-OH) group for activity.

Figure 5 shows an example of a DNAzyme motif described by Santoro *et al.*, 1997, *PNAS*, 94, 4262.

Figure 6 is a bar graph showing the percent change in serum HBV DNA levels following fourteen days of ribozyme treatment in HBV transgenic mice. Ribozymes targeting sites 273 (RPI.18341) and 1833 (RPI.18371) of HBV RNA administered via continuous s.c. infusion at 10, 30, and 100 mg/kg/day are compared to continuous s.c. infusion administration of scrambled attenuated core ribozyme and saline controls, and orally administered 3TC® (300 mg/kg/day) and saline controls.

Figure 7 is a bar graph showing the mean serum HBV DNA levels following fourteen days of ribozyme treatment in HBV transgenic mice. Ribozymes targeting sites 273 (RPI.18341) and 1833 (RPI.18371) of HBV RNA administered via continuous s.c. infusion at 10, 30, and 100 mg/kg/day are compared to continuous s.c. infusion administration of scrambled attenuated core ribozyme and saline controls, and orally administered 3TC® (300 mg/kg/day) and saline controls.

Figure 8 is a bar graph showing the decrease in serum HBV DNA (log) levels following fourteen days of ribozyme treatment in HBV transgenic mice. Ribozymes targeting sites 273 (RPI.18341) and 1833 (RPI.18371) of HBV RNA administered via continuous s.c. infusion at 10, 30, and 100 mg/kg/day are compared to continuous s.c. infusion administration of scrambled attenuated core ribozyme and saline controls, and orally administered 3TC® (300 mg/kg/day) and saline controls.

Figure 9 is a bar graph showing the decrease in HBV DNA in HepG2.2.15 cells after treatment with ribozymes targeting sites 273 (RPI.18341), 1833 (RPI.18371), 1874

(RPI.18372), and 1873 (RPI.18418) of HBV RNA as compared to a scrambled attenuated core ribozyme (RPI.20995).

Figure 10 is a bar graph showing reduction in HBsAg levels following treatment of HepG2 cells with anti-HBV arm, stem, and loop-variant ribozymes (RPI.18341, RPI.22644, RPI.22645, RPI.22646, RPI.22647, RPI.22648, RPI.22649, and RPI.22650) targeting site 273 of the HBV pregenomic RNA as compared to a scrambled attenuated core ribozyme (RPI.20599).

Figure 11 is a bar graph showing reduction in HBsAg levels following treatment of HepG2 cells with RPI 18341 alone or in combination with Infergen®. At either 500 or 1000 units of Infergen®, the addition of 200 nM of RPI.18341 results in a 75-77% increase in anti-HBV activity as judged by the level of HBsAg secreted from the treated Hep G2 cells. Conversely, the anti-HBV activity of RPI.18341(at 200 nM) is increased 31-39% when used in combination of 500 or 1000 units of Infergen®.

Figure 12 is a bar graph showing reduction in HBsAg levels following treatment of HepG2 cells with RPI 18341 alone or in combination with Lamivudine. At 25 nM Lamivudine (3TC®), the addition of 100 nM of RPI.18341 results in a 48% increase in anti-HBV activity as judged by the level of HBsAg secreted from treated Hep G2 cells. Conversely, the anti-HBV activity of RPI.18341 (at 100 nM) is increased 31% when used in combination with 25 nM Lamivudine.

Figure 13 shows a scheme which outlines the steps involved in HBV reverse transcription. The HBV polymerase/reverse transcriptase binds to the 5'-stem-loop of the HBV pregenomic RNA and synthesizes a primer from the UUCA template. The reverse transcriptase and tetramer primer are translocated to the 3'-DR1 site. The RT primer binds to the UUCA sequence in the DR1 element and minus strand synthesis begins.

Figure 14 shows a non-limiting example of inhibition of HBV reverse transcription. A decoy molecule binds to the HBV RT primer, thereby preventing translocation of the RT to the 3'-DR1 site and preventing minus strand synthesis.

Figure 15 shows data of a HBV nucleic acid screen of 2'-O-allyl modified nucleic acid molecules. The levels of HbsAg were determined by ELISA. Inhibition of HBV is correlated to HBsAg antigen levels.

Figure 16 shows data of a HBV nucleic acid screen of 2'-O-methyl modified nucleic acid molecules. The levels of HbsAg were determined by ELISA. Inhibition of HBV is correlated to HBsAg antigen levels.

Figure 17 shows dose response data of 2'-O-methyl modified nucleic acid molecules targeting the HBV reverse transcriptase primer compared to levels of HBsAg.

Figure 18 shows data of nucleic acid screen of nucleic acid molecules (200 nM) targeting the HBV Enhancer I core region compared to levels of HBsAg.

Figure 19 shows data of nucleic acid screen of nucleic acid molecules (400 nM) targeting the HBV Enhancer I core region compared to levels of HBsAg.

Figure 20 shows dose response data of nucleic acid molecules targeting the HBV Enhancer I core region compared to levels of HBsAg.

Figure 21 shows a graph depicting HepG2.2.15 tumor growth in athymic nu/nu female mice as tumor volume (mm³) vs time (days).

Figure 22 shows a graph depicting HepG2.2.15 tumor growth in athymic nu/nu female mice as tumor volume (mm³) vs time (days). Inoculated HepG2.2.15 cells were selected for antibiotic resistance to G418 before introduction into the mouse.

Figure 23 is a schematic representation of the Dual Reporter System utilized to demonstrate enzymatic nucleic acid mediated reduction of luciferase activity in cell culture.

Figure 24 shows a schematic view of the secondary structure of the HCV 5'UTR (Brown *et al.*, 1992, *Nucleic Acids Res.*, 20, 5041-45; Honda *et al.*, 1999, *J. Virol.*, 73, 1165-74). Major structural domains are indicated in bold. Enzymatic nucleic acid cleavage sites are indicated by arrows. Solid arrows denote sites amenable to amino-modified enzymatic nucleic acid inhibition. Lead cleavage sites (195 and 330) are indicated with oversized solid arrows.

Figure 25 shows a non-limiting example of a nuclease resistant enzymatic nucleic acid molecule. Binding arms are indicated as stem I and stem III. Nucleotide modifications are indicated as follows: 2'-O-methyl nucleotides, lowercase; ribonucleotides, uppercase G, A; 2'-amino-uridine, u; inverted 3'-3' deoxyabasic, **B**. The positions of phosphorothioate linkages at the 5'-end of each enzymatic nucleic acid are indicated by subscript "s". *H* indicates A, C or U ribonucleotide, *N'* indicates A, C G or U ribonucleotide in substrate, *n* indicates base complementary to the *N'*. The U4 and U7 positions in the catalytic core are indicated.

Figure 26 is a set of bar graphs showing enzymatic nucleic acid mediated inhibition of HCV-luciferase expression in OST7 cells. OST7 cells were transfected with complexes containing reporter plasmids (2 µg/mL), enzymatic nucleic acids (100 nM) and lipid. The ratio of HCV-firefly luciferase luminescence/Renilla luciferase luminescence was determined

for each enzymatic nucleic acid tested and was compared to treatment with the ICR, an irrelevant control enzymatic nucleic acid lacking specificity to the HCV 5'UTR (adjusted to 1). Results are reported as the mean of triplicate samples \pm SD. In **Figure 26A**, OST7 cells were treated with enzymatic nucleic acids (100 nM) targeting conserved sites (indicated by cleavage site) within the HCV 5'UTR. In **Figure 26B**, OST7 cells were treated with a subset of enzymatic nucleic acids to lead HCV sites (indicated by cleavage site) and corresponding attenuated core (AC) controls. Percent decrease in firefly/Renilla luciferase ratio after treatment with active enzymatic nucleic acids as compared to treatment with corresponding ACs is shown when the decrease is $\geq 50\%$ and statistically significant. Similar results were obtained with 50 nM enzymatic nucleic acid.

Figure 27 is a series of line graphs showing the dose-dependent inhibition of HCV/luciferase expression following enzymatic nucleic acid treatment. Active enzymatic nucleic acid was mixed with corresponding AC to maintain a 100 nM total oligonucleotide concentration and the same lipid charge ratio. The concentration of active enzymatic nucleic acid for each point is shown. **Figure 27A–E** shows enzymatic nucleic acids targeting sites 79, 81, 142, 195, or 330, respectively. Results are reported as the mean of triplicate samples \pm SD.

Figure 28 is a set of bar graphs showing reduction of HCV/luciferase RNA and inhibition of HCV-luciferase expression in OST7 cells. OST7 cells were transfected with complexes containing reporter plasmids (2 μ g /ml), enzymatic nucleic acids, BACs or SACs (50 nM) and lipid. Results are reported as the mean of triplicate samples \pm SD. In **Figure 28A** the ratio of HCV-firefly luciferase RNA/Renilla luciferase RNA is shown for each enzymatic nucleic acid or control tested. As compared to paired BAC controls (adjusted to 1), luciferase RNA levels were reduced by 40% and 25% for the site 195 or 330 enzymatic nucleic acids, respectively. In **Figure 28B** the ratio of HCV-firefly luciferase luminescence/Renilla luciferase luminescence is shown after treatment with site 195 or 330 enzymatic nucleic acids or paired controls. As compared to paired BAC controls (adjusted to 1), inhibition of protein expression was 70% and 40% for the site 195 or 330 enzymatic nucleic acids, respectively $P < 0.01$.

Figure 29 is a set a bar graphs showing interferon (IFN) alpha 2a and 2b dose response in combination with site 195 anti-HCV enzymatic nucleic acid treatment. **Figure 29A** shows data for IFN alfa 2a treatment. **Figure 29B** shows data for IFN alfa 2b treatment. Viral yield is reported from HeLa cells pretreated with IFN in units/ml (U/ml) as indicated for 4 h prior to infection and then treated with either 200 nM control (SAC) or site 195 anti-HCV enzymatic nucleic acid (195 RZ) for 24 h after infection. Cells were infected with a MOI =

0.1 for 30 min and collected at 24 h post infection. Error bars represent the S.D. of the mean of triplicate determinations.

Figure 30 is a line graph showing site 195 anti-HCV enzymatic nucleic acid dose response in combination with interferon (IFN) alpha 2a and 2b pretreatment. Viral yield is reported from HeLa cells pretreated for 4 h with or without IFN and treated with doses of site 195 anti-HCV enzymatic nucleic acid (195 RZ) as indicated for 24 h after infection. Anti-HCV enzymatic nucleic acid was mixed with control oligonucleotide (SAC) to maintain a constant 200 nM total dose of nucleic acid for delivery. Cells were infected with a MOI = 0.1 for 30 min and collected at 24 h post infection. Error bars represent the S.D. of the mean of triplicate determinations.

Figure 31 is a set of bar graphs showing data from consensus interferon (CIFN)/enzymatic nucleic acid combination treatment. **Figure 31A** shows CIFN dose response with site 195 anti-HCV enzymatic nucleic acid treatment. Viral yield is reported from cells pretreated with CIFN in units/ml (U/ml) as indicated and treated with either 200 nM control (SAC) or site 195 anti-HCV enzymatic nucleic acid (195 RZ). **Figure 31B** shows site 195 anti-HCV enzymatic nucleic acid dose response with CIFN pretreatment. Viral yield is reported from cells pretreated with or without CIFN and treated with concentrations of site 195 anti-HCV enzymatic nucleic acid (195 RZ) as indicated. Anti-HCV enzymatic nucleic acid was mixed with control oligonucleotide (SAC) to maintain a constant 200 nM total dose of nucleic acid for delivery. Cells were infected with a MOI = 0.1 for 30 min. and collected at 24 h post infection. Error bars represent the S.D. of the mean of triplicate determinations.

Figure 32 is a bar graph showing enzymatic nucleic acid activity and enhanced antiviral effect of an anti-HCV enzymatic nucleic acid targeting site 195 used in combination with consensus interferon (CIFN). Viral yield is reported from cells treated as indicated. BAC, cells were treated with 200 nM BAC (binding attenuated control) for 24 h after infection; CIFN+BAC, cells were treated with 12.5 U/ml CIFN for 4 h prior to infection and with 200 nM BAC for 24 h after infection; 195 RZ, cells were treated with 200 nM site 195 anti-HCV enzymatic nucleic acid for 24 h after infection; CIFN + 195 RZ, cells were treated with 12.5 U/ml CIFN for 4 h prior to infection and with 200 nM site 195 anti-HCV enzymatic nucleic acid for 24 h after infection. Cells were infected with a MOI = 0.1 for 30 min. Error bars represent the S.D. of the mean of triplicate determinations.

Figure 33 is a bar graph showing inhibition of a HCV-PV chimera replication by treatment with zinzyme enzymatic nucleic acid molecules targeting different sites within the HCV 5'-UTR compared to a scrambled attenuated core control (SAC) zinzyme.

Figure 34 is a bar graph showing inhibition of a HCV-PV chimera replication by antisense nucleic acid molecules targeting conserved regions of the HCV 5'-UTR compared to scrambled antisense controls.

Figure 35 shows the structure of compounds (2-5A) utilized in the study. "X" denotes the position of oxygen (O) in analog I or sulfur (S) in thiophosphate (P=S) analog II. The 2-5A compounds were synthesized, deprotected and purified as described herein utilizing CPG support with 3'-inverted abasic nucleotide. For chain extension 5'-O-(4,4'-dimethoxytrityl)-3'-O-(tert-butyldimethylsilyl)-N6-benzoyladenosine-2-cyanoethyl-N,N-diisopropyl-phosphoramidite (Chem. Genes Corp., Waltham, MA) was employed. Introduction of a 5'-terminal phosphate (analog I) or thiophosphate (analog II) group was performed with "Chemical Phosphorylation Reagent" (Glen Research, Sterling, VA). Structures of the final compounds were confirmed by MALDI-TOF analysis.

Figure 36 is a bar graph showing ribozyme activity and enhanced antiviral effect. (A) Interferon/ribozyme combination treatment. (B) 2-5A/ribozyme combination treatment. HeLa cells seeded in 96-well plates (10,000 cells per well) were pretreated as indicated for 4 hours. For pretreatment, SAC (RPI 17894), RZ (RPI 13919), and 2-5A analog I (RPI 21096) (200 nM) were complexed with lipid cytofectin. Cells were then infected with HCV-PV at a multiplicity of infection of 0.1. Virus inoculum was replaced after 30 minutes with media containing 5% serum and 100 nM RZ or SAC as indicated, complexed with cytofectin RPI.9778. After 20 hours, cells were lysed by 3 freeze/thaw cycles and virus was quantified by plaque assay. Plaque forming units (PFU)/ml are shown as the mean of triplicate samples + SEM. The absolute amount of viral yield in treated cells varied from day to day, presumably due to day to day variations in cell plating and transfection complexation. None, normal media; IFN, 10 U/ml consensus interferon; SAC, scrambled arm attenuated core control (RPI 17894); RZ, anti-HCV ribozyme (RPI 13919); 2-5A, (RPI 21096).

Figure 37 is a graph showing the inhibition of viral replication with anti-HCV ribozyme (RPI 13919) or 2-5A (RPI 21096) treatment. HeLa cells were treated as described in **Figure 36** except that there was no pretreatment and 200 nM oligonucleotide was used for treatment. 2-5A P=S contains a 5'-terminal thiophosphate (RPI21095) (see **Figure 35**).

Figure 38 is a bar graph showing anti-HCV ribozyme in combination with 2-5A treatment. HeLa cells were treated as described in **Figure 37** except concentrations were co-varied as shown to maintain a constant 200 nM total oligonucleotide dose for transfection. Cells treated with 50 nM anti-HCV ribozyme (RPI 13919) (middle bars) were also treated with 150 nM SAC (RPI 17894) or 2-5A (RPI 21096); likewise, cells treated with 100 nM anti-HCV ribozyme (bars at right) were also treated with 100 nM SAC or 2-5A.

Mechanism of action of Nucleic Acid Molecules of the Invention

Decoy: Nucleic acid decoy molecules are mimetics of naturally occurring nucleic acid molecules or portions of naturally occurring nucleic acid molecules that can be used to modulate the function of a specific protein or a nucleic acid whose activity is dependant on interaction with the naturally occurring nucleic acid molecule. Decoys modulate the function of a target protein or nucleic acid by competing with authentic nucleic acid binding to the ligand of interest. Often, the nucleic acid decoy is a truncated version of a nucleic acid sequence that is recognized, for example by a particular protein, such as a transcription factor or polymerase. Decoys can be chemically modified to increase binding affinity to the target ligand as well as to increase the enzymatic and chemical stability of the decoy. In addition, bridging and non-bridging linkers can be introduced into the decoy sequence to provide additional binding affinity to the target ligand. Decoy molecules of the invention that bind to an HCV or HBV target, such as HBV reverse transcriptase or HBV reverse transcriptase primer, or an enhancer region of the HBV pregenomic RNA, for example the Enhancer I element, modulate the transcription of RNA to DNA and therefore modulate expression of the pregenomic RNA of the virus (see **Figures 13 and 14**).

Aptamer: Nucleic acid aptamers can be selected to specifically bind to a particular ligand of interest (see for example Gold *et al.*, US 5,567,588 and US 5,475,096, Gold *et al.*, 1995, *Annu. Rev. Biochem.*, 64, 763; Brody and Gold, 2000, *J. Biotechnol.*, 74, 5; Sun, 2000, *Curr. Opin. Mol. Ther.*, 2, 100; Kusser, 2000, *J. Biotechnol.*, 74, 27; Hermann and Patel, 2000, *Science*, 287, 820; and Jayasena, 1999, *Clinical Chemistry*, 45, 1628). For example, the use of in vitro selection can be applied to evolve nucleic acid aptamers with binding specificity for HBV RT and/or HBV RT primer. Nucleic acid aptamers can include chemical modifications and linkers as described herein. Aptamer molecules of the invention that bind to a reverse transcriptase or reverse transcriptase primer, such as HBV reverse transcriptase or HBV reverse transcriptase primer, modulate the transcription of RNA to DNA and therefore modulate expression of the pregenomic RNA of the virus.

Antisense: Antisense molecules can be modified or unmodified RNA, DNA, or mixed polymer oligonucleotides and primarily function by specifically binding to matching sequences resulting in modulation of peptide synthesis (Wu-Pong, Nov 1994, *BioPharm*, 20-33). The antisense oligonucleotide binds to target RNA by Watson Crick base-pairing and blocks gene expression by preventing ribosomal translation of the bound sequences either by steric blocking or by activating RNase H enzyme. Antisense molecules can also alter protein synthesis by interfering with RNA processing or transport from the nucleus into the cytoplasm (Mukhopadhyay & Roth, 1996, *Crit. Rev. in Oncogenesis* 7, 151-190).

In addition, binding of single stranded DNA to RNA may result in nuclease degradation of the heteroduplex (Wu-Pong, *supra*; Crooke, *supra*). To date, the only backbone modified DNA chemistry which will act as substrates for RNase H are phosphorothioates, phosphorodithioates, and borontrifluoridates. Recently, it has been reported that 2'-arabino and 2'-fluoro arabino- containing oligos can also activate RNase H activity.

A number of antisense molecules have been described that utilize novel configurations of chemically modified nucleotides, secondary structure, and/or RNase H substrate domains (Woolf *et al.*, International PCT Publication No. WO 98/13526; Thompson *et al.*, USSN 60/082,404 which was filed on April 20, 1998; Hartmann *et al.*, USSN 60/101,174 which was filed on September 21, 1998) all of these are incorporated by reference herein in their entirety.

Antisense DNA can be used to target RNA by means of DNA-RNA interactions, thereby activating RNase H, which digests the target RNA in the duplex. Antisense DNA can be chemically synthesized or can be expressed via the use of a single stranded DNA intracellular expression vector or the equivalent thereof.

Triplex Forming Oligonucleotides (TFO): Single stranded oligonucleotide can be designed to bind to genomic DNA in a sequence specific manner. TFOs can be comprised of pyrimidine-rich oligonucleotides which bind DNA helices through Hoogsteen Base-pairing (Wu-Pong, *supra*). In addition, TFOs can be chemically modified to increase binding affinity to target DNA sequences. The resulting triple helix composed of the DNA sense, DNA antisense, and TFO disrupts RNA synthesis by RNA polymerase. The TFO mechanism can result in gene expression or cell death since binding may be irreversible (Mukhopadhyay & Roth, *supra*)

2'-5' Oligoadenylates: The 2-5A system is an interferon-mediated mechanism for RNA degradation found in higher vertebrates (Mitra *et al.*, 1996, *Proc Nat Acad Sci USA* 93, 6780-6785). Two types of enzymes, 2-5A synthetase and RNase L, are required for RNA cleavage. The 2-5A synthetases require double stranded RNA to form 2'-5' oligoadenylates (2-5A). 2-5A then acts as an allosteric effector for utilizing RNase L, which has the ability to cleave single stranded RNA. The ability to form 2-5A structures with double stranded RNA makes this system particularly useful for modulation of viral replication.

(2'-5') oligoadenylate structures can be covalently linked to antisense molecules to form chimeric oligonucleotides capable of RNA cleavage (Torrence, *supra*). These molecules putatively bind and activate a 2-5A-dependent RNase, the oligonucleotide/enzyme complex then binds to a target RNA molecule which can then be cleaved by the RNase enzyme. The covalent attachment of 2'-5' oligoadenylate structures is not limited to

antisense applications, and can be further elaborated to include attachment to nucleic acid molecules of the instant invention.

RNA interference (RNAi): RNA interference refers to the process of sequence specific post transcriptional gene silencing in animals mediated by short interfering RNAs (siRNA) (Fire *et al.*, 1998, *Nature*, 391, 806). The corresponding process in plants is commonly referred to as post transcriptional gene silencing or RNA silencing and is also referred to as quelling in fungi. The process of post transcriptional gene silencing is thought to be an evolutionarily conserved cellular defense mechanism used to prevent the expression of foreign genes which is commonly shared by diverse flora and phyla (Fire *et al.*, 1999, *Trends Genet.*, 15, 358). Such protection from foreign gene expression may have evolved in response to the production of double stranded RNAs (dsRNA) derived from viral infection or the random integration of transposon elements into a host genome via a cellular response that specifically destroys homologous single stranded RNA or viral genomic RNA. The presence of dsRNA in cells triggers the RNAi response through a mechanism that has yet to be fully characterized. This mechanism appears to be different from the interferon response that results from dsRNA mediated activation of protein kinase PKR and 2',5'-oligoadenylate synthetase resulting in non-specific cleavage of mRNA by ribonuclease L.

The presence of long dsRNAs in cells stimulates the activity of a ribonuclease III enzyme referred to as dicer. Dicer is involved in the processing of the dsRNA into short pieces of dsRNA known as short interfering RNAs (siRNA) (Berstein *et al.*, 2001, *Nature*, 409, 363). Short interfering RNAs derived from dicer activity are typically about 21-23 nucleotides in length and comprise about 19 base pair duplexes. Dicer has also been implicated in the excision of 21 and 22 nucleotide small temporal RNAs (stRNA) from precursor RNA of conserved structure that are implicated in translational control (Hutvagner *et al.*, 2001, *Science*, 293, 834). The RNAi response also features an endonuclease complex containing a siRNA, commonly referred to as an RNA-induced silencing complex (RISC), which mediates cleavage of single stranded RNA having sequence homologous to the siRNA. Cleavage of the target RNA takes place in the middle of the region complementary to the guide sequence of the siRNA duplex (Elbashir *et al.*, 2001, *Genes Dev.*, 15, 188).

Short interfering RNA mediated RNAi has been studied in a variety of systems. Fire *et al.*, 1998, *Nature*, 391, 806, were the first to observe RNAi in *C. Elegans*. Wianny and Goetz, 1999, *Nature Cell Biol.*, 2, 70, describes RNAi mediated by dsRNA in mouse embryos. Hammond *et al.*, 2000, *Nature*, 404, 293, describe RNAi in *Drosophila* cells transfected with dsRNA. Elbashir *et al.*, 2001, *Nature*, 411, 494, describe RNAi induced by introduction of duplexes of synthetic 21-nucleotide RNAs in cultured mammalian cells including human embryonic kidney and HeLa cells. Recent work in *Drosophila* embryonic lysates has revealed certain requirements for siRNA length, structure, chemical composition,

and sequence that are essential to mediate efficient RNAi activity. These studies have shown that 21 nucleotide siRNA duplexes are most active when containing two nucleotide 3'-overhangs. Furthermore, substitution of one or both siRNA strands with 2'-deoxy or 2'-O-methyl nucleotides abolishes RNAi activity, whereas substitution of 3'-terminal siRNA nucleotides with deoxy nucleotides was shown to be tolerated. Mismatch sequences in the center of the siRNA duplex were also shown to abolish RNAi activity. In addition, these studies also indicate that the position of the cleavage site in the target RNA is defined by the 5'-end of the siRNA guide sequence rather than the 3'-end (Elbashir *et al.*, 2001, *EMBO J.*, 20, 6877). Other studies have indicated that a 5'-phosphate on the target-complementary strand of a siRNA duplex is required for siRNA activity and that ATP is utilized to maintain the 5'-phosphate moiety on the siRNA (Nykanen *et al.*, 2001, *Cell*, 107, 309), however siRNA molecules lacking a 5'-phosphate are active when introduced exogenously, suggesting that 5'-phosphorylation of siRNA constructs may occur *in vivo*.

Enzymatic Nucleic Acid: Several varieties of naturally occurring enzymatic RNAs are presently known (Doherty and Doudna, 2001, *Annu. Rev. Biophys. Biomol. Struct.*, 30, 457-475; Symons, 1994, *Curr. Opin. Struct. Biol.*, 4, 322-30). In addition, several *in vitro* selection (evolution) strategies (Orgel, 1979, *Proc. R. Soc. London*, B 205, 435) have been used to evolve new nucleic acid catalysts capable of catalyzing cleavage and ligation of phosphodiester linkages (Joyce, 1989, *Gene*, 82, 83-87; Beaudry *et al.*, 1992, *Science* 257, 635-641; Joyce, 1992, *Scientific American* 267, 90-97; Breaker *et al.*, 1994, *TIBTECH* 12, 268; Bartel *et al.*, 1993, *Science* 261:1411-1418; Szostak, 1993, *TIBS* 17, 89-93; Kumar *et al.*, 1995, *FASEB J.*, 9, 1183; Breaker, 1996, *Curr. Op. Biotech.*, 7, 442; Santoro *et al.*, 1997, *Proc. Natl. Acad. Sci.*, 94, 4262; Tang *et al.*, 1997, *RNA* 3, 914; Nakamaye & Eckstein, 1994, *supra*; Long & Uhlenbeck, 1994, *supra*; Ishizaka *et al.*, 1995, *supra*; Vaish *et al.*, 1997, *Biochemistry* 36, 6495). Each can catalyze a series of reactions including the hydrolysis of phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions.

Nucleic acid molecules of this invention can block HBV or HCV protein expression and can be used to treat disease or diagnose disease associated with the levels of HBV or HCV.

The enzymatic nature of an enzymatic nucleic acid has significant advantages, such as the concentration of nucleic acid necessary to affect a therapeutic treatment is low. This advantage reflects the ability of the enzymatic nucleic acid molecule to act enzymatically. Thus, a single enzymatic nucleic acid molecule is able to cleave many molecules of target RNA. In addition, the enzymatic nucleic acid molecule is a highly specific modulator, with the specificity of modulation depending not only on the base-pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches,

or base-substitutions, near the site of cleavage can be chosen to completely eliminate catalytic activity of an enzymatic nucleic acid molecule.

Nucleic acid molecules having an endonuclease enzymatic activity are able to repeatedly cleave other separate RNA molecules in a nucleotide base sequence-specific manner. With proper design and construction, such enzymatic nucleic acid molecules can be targeted to any RNA transcript, and efficient cleavage achieved *in vitro* (Zaug *et al.*, 324, *Nature* 429 1986; Uhlenbeck, 1987 *Nature* 328, 596; Kim *et al.*, 84 *Proc. Natl. Acad. Sci. USA* 8788, 1987; Dreyfus, 1988, *Einstein Quart. J. Bio. Med.*, 6, 92; Haseloff and Gerlach, 334 *Nature* 585, 1988; Cech, 260 *JAMA* 3030, 1988; and Jefferies *et al.*, 17 *Nucleic Acids Research* 1371, 1989; Chartrand *et al.*, 1995, *Nucleic Acids Research* 23, 4092; Santoro *et al.*, 1997, *PNAS* 94, 4262).

Because of their sequence specificity, *trans*-cleaving enzymatic nucleic acid molecules show promise as therapeutic agents for human disease (Usman & McSwiggen, 1995 *Ann. Rep. Med. Chem.* 30, 285-294; Christoffersen and Marr, 1995 *J. Med. Chem.* 38, 2023-2037). Enzymatic nucleic acid molecule can be designed to cleave specific RNA targets within the background of cellular RNA. Such a cleavage event renders the RNA non-functional and abrogates protein expression from that RNA. In this manner, synthesis of a protein associated with a disease state can be selectively modulated (Warashina *et al.*, 1999, *Chemistry and Biology*, 6, 237-250).

The present invention also features nucleic acid sensor molecules or allozymes having sensor domains comprising nucleic acid decoys and/or aptamers of the invention. Interaction of the nucleic acid sensor molecule's sensor domain with a molecular target, such as HCV or HBV target, e.g., HBV RT and/or HBV RT primer, can activate or inactivate the enzymatic nucleic acid domain of the nucleic acid sensor molecule, such that the activity of the nucleic acid sensor molecule is modulated in the presence of the target-signaling molecule. The nucleic acid sensor molecule can be designed to be active in the presence of the target molecule or alternately, can be designed to be inactive in the presence of the molecular target. For example, a nucleic acid sensor molecule is designed with a sensor domain having the sequence (UUC_A)_n, where n is an integer from 1-10. In a non-limiting example, interaction of the HBV RT primer with the sensor domain of the nucleic acid sensor molecule can activate the enzymatic nucleic acid domain of the nucleic acid sensor molecule such that the sensor molecule catalyzes a reaction, for example cleavage of HBV RNA. In this example, the nucleic acid sensor molecule is activated in the presence of HBV RT or HBV RT primer, and can be used as a therapeutic to treat HBV infection. Alternately, the reaction can comprise cleavage or ligation of a labeled nucleic acid reporter molecule, providing a useful diagnostic reagent to detect the presence of HBV in a system.

HCV Target sites

Targets for useful nucleic acid molecules and nuclease activating compounds or chimeras can be determined as disclosed in Draper *et al.*, WO 93/23569; Sullivan *et al.*, WO 93/23057; Thompson *et al.*, WO 94/02595; Draper *et al.*, WO 95/04818; McSwiggen *et al.*, US Patent No. 5,525,468. Rather than repeat the guidance provided in those documents here, below are provided specific examples of such methods, not limiting to those in the art. Nucleic acid molecules and nuclease activating compounds or chimeras to such targets are designed as described in those applications and synthesized to be tested *in vitro* and *in vivo*, as also described. Such nucleic acid molecules and nuclease activating compounds or chimeras can also be optimized and delivered as described therein.

The sequence of HCV RNAs were screened for optimal enzymatic nucleic acid molecule target sites using a computer folding algorithm. Enzymatic nucleic acid cleavage sites were identified. These sites are shown in Tables XVIII, XIX, XX and XXIII (All sequences are 5' to 3' in the tables). The nucleotide base position is noted in the tables as that site to be cleaved by the designated type of enzymatic nucleic acid molecule. The nucleotide base position is noted in the tables as that site to be cleaved by the designated type of enzymatic nucleic acid molecule.

Because HCV RNAs are highly homologous in certain regions, some enzymatic nucleic acid molecule target sites are also homologous. In this case, a single enzymatic nucleic acid molecule will target different classes of HCV RNA. The advantage of one enzymatic nucleic acid molecule that targets several classes of HCV RNA is clear, especially in cases where one or more of these RNAs can contribute to the disease state.

Enzymatic nucleic acid molecules were designed that could bind and were individually analyzed by computer folding (Jaeger *et al.*, 1989 *Proc. Natl. Acad. Sci. USA*, 86, 7706) to assess whether the enzymatic nucleic acid molecule sequences fold into the appropriate secondary structure. Those enzymatic nucleic acid molecules with unfavorable intramolecular interactions between the binding arms and the catalytic core are eliminated from consideration. Varying binding arm lengths can be chosen to optimize activity. Generally, at least 5 bases on each arm are able to bind to, or otherwise interact with, the target RNA. Enzymatic nucleic acid molecules were designed to anneal to various sites in the mRNA message. The binding arms are complementary to the target site sequences described above.

HBV Target sites

Targets for useful ribozymes and antisense nucleic acids targeting HBV can be determined as disclosed in Draper *et al.*, WO 93/23569; Sullivan *et al.*, WO 93/23057; Thompson *et al.*, WO 94/02595; Draper *et al.*, WO 95/04818; McSwiggen *et al.*, US Patent No. 5,525,468. Other examples include the following PCT applications, which concern inactivation of expression of disease-related genes: WO 95/23225, WO 95/13380, WO 94/02595. Rather than repeat the guidance provided in those documents here, below are provided specific examples of such methods; not limiting to those in the art. Ribozymes and antisense to such targets are designed as described in those applications and synthesized to be tested *in vitro* and *in vivo*, as also described. The sequence of human HBV RNAs (for example, accession AF100308.1; HBV strain 2-18; additionally, other HBV strains can be screened by one skilled in the art, see Table III for other possible strains) were screened for optimal enzymatic nucleic acid and antisense target sites using a computer-folding algorithm. Antisense, hammerhead, DNAzyme, NCH (Inozyme), amberzyme, zinzyme or G-Cleaver ribozyme binding/cleavage sites were identified. These sites are shown in Tables V to XI (all sequences are 5' to 3' in the tables; X can be any base-paired sequence, the actual sequence is not relevant here). The nucleotide base position is noted in the Tables as that site to be cleaved by the designated type of enzymatic nucleic acid molecule. Table IV shows substrate positions selected from Renbo *et al.*, 1987, *Sci. Sin.*, 30, 507, used in Draper, USSN (07/882,712), filed May 14, 1992, entitled "METHOD AND REAGENT FOR INHIBITING HEPATITIS B VIRUS REPLICATION" and Draper *et al.*, International PCT publication No. WO 93/23569, filed April 29, 1993, entitled "METHOD AND REAGENT FOR INHIBITING VIRAL REPLICATION". While human sequences can be screened and enzymatic nucleic acid molecule and/or antisense thereafter designed, as discussed in Stinchcomb *et al.*, WO 95/23225, mouse targeted ribozymes can be useful to test efficacy of action of the enzymatic nucleic acid molecule and/or antisense prior to testing in humans.

Antisense, hammerhead, DNAzyme, NCH (Inozyme), amberzyme, zinzyme or G-Cleaver ribozyme binding/cleavage sites were identified, as discussed above. The nucleic acid molecules were individually analyzed by computer folding (Jaeger *et al.*, 1989 *Proc. Natl. Acad. Sci. USA*, 86, 7706) to assess whether the sequences fold into the appropriate secondary structure. Those nucleic acid molecules with unfavorable intramolecular interactions such as between the binding arms and the catalytic core were eliminated from consideration. Varying binding arm lengths can be chosen to optimize activity.

Antisense, hammerhead, DNAzyme, NCH, amberzyme, zinzyme or G-Cleaver ribozyme binding/cleavage sites were identified and were designed to anneal to various sites in the RNA target. The binding arms are complementary to the target site sequences

described above. The nucleic acid molecules were chemically synthesized. The method of synthesis used follows the procedure for normal DNA/RNA synthesis as described below and in Usman *et al.*, 1987 *J. Am. Chem. Soc.*, 109, 7845; Scaringe *et al.*, 1990 *Nucleic Acids Res.*, 18, 5433; Wincott *et al.*, 1995 *Nucleic Acids Res.* 23, 2677-2684; and Caruthers *et al.*, 1992, *Methods in Enzymology* 211,3-19.

Synthesis of Nucleic acid Molecules

Synthesis of nucleic acids greater than 100 nucleotides in length is difficult using automated methods, and the therapeutic cost of such molecules is prohibitive. In this invention, small nucleic acid motifs ("small" refers to nucleic acid motifs no more than 100 nucleotides in length, preferably no more than 80 nucleotides in length, and most preferably no more than 50 nucleotides in length; e.g., decoy nucleic acid molecules, aptamer nucleic acid molecules antisense nucleic acid molecules, enzymatic nucleic acid molecules) are preferably used for exogenous delivery. The simple structure of these molecules increases the ability of the nucleic acid to invade targeted regions of protein and/or RNA structure. Exemplary molecules of the instant invention are chemically synthesized, and others can similarly be synthesized.

Oligonucleotides (e.g., DNA oligonucleotides) are synthesized using protocols known in the art, for example as described in Caruthers *et al.*, 1992, *Methods in Enzymology* 211, 3-19, Thompson *et al.*, International PCT Publication No. WO 99/54459, Wincott *et al.*, 1995, *Nucleic Acids Res.* 23, 2677-2684, Wincott *et al.*, 1997, *Methods Mol. Bio.*, 74, 59, Brennan *et al.*, 1998, *Biotechnol Bioeng.*, 61, 33-45, and Brennan, US patent No. 6,001,311. The synthesis of oligonucleotides makes use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. In a non-limiting example, small scale syntheses are conducted on a 394 Applied Biosystems, Inc. synthesizer using a 0.2 μmol scale protocol with a 2.5 min coupling step for 2'-O-methylated nucleotides and a 45 sec coupling step for 2'-deoxy nucleotides. **Table II** outlines the amounts and the contact times of the reagents used in the synthesis cycle. Alternatively, syntheses at the 0.2 μmol scale can be performed on a 96-well plate synthesizer, such as the instrument produced by Protogene (Palo Alto, CA) with minimal modification to the cycle. A 33-fold excess (60 μL of 0.11 M = 6.6 μmol) of 2'-O-methyl phosphoramidite and a 105-fold excess of S-ethyl tetrazole (60 μL of 0.25 M = 15 μmol) can be used in each coupling cycle of 2'-O-methyl residues relative to polymer-bound 5'-hydroxyl. A 22-fold excess (40 μL of 0.11 M = 4.4 μmol) of deoxy phosphoramidite and a 70-fold excess of S-ethyl tetrazole (40 μL of 0.25 M = 10 μmol) can be used in each coupling cycle of deoxy residues relative to polymer-bound 5'-hydroxyl. Average coupling yields on the 394 Applied Biosystems, Inc. synthesizer, determined by colorimetric quantitation of the trityl fractions, are typically 97.5-

99%. Other oligonucleotide synthesis reagents for the 394 Applied Biosystems, Inc. synthesizer include the following: detritylation solution is 3% TCA in methylene chloride (ABI); capping is performed with 16% *N*-methyl imidazole in THF (ABI) and 10% acetic anhydride/10% 2,6-lutidine in THF (ABI); and oxidation solution is 16.9 mM I₂, 49 mM pyridine, 9% water in THF (PERSEPTIVE™). Burdick & Jackson Synthesis Grade acetonitrile is used directly from the reagent bottle. S-Ethyltetrazole solution (0.25 M in acetonitrile) is made up from the solid obtained from American International Chemical, Inc. Alternately, for the introduction of phosphorothioate linkages, Beaucage reagent (3H-1,2-Benzodithiol-3-one 1,1-dioxide, 0.05 M in acetonitrile) is used.

Deprotection of the DNA-based oligonucleotides is performed as follows: the polymer-bound trityl-on oligoribonucleotide is transferred to a 4 mL glass screw top vial and suspended in a solution of 40% aq. methylamine (1 mL) at 65 °C for 10 min. After cooling to -20 °C, the supernatant is removed from the polymer support. The support is washed three times with 1.0 mL of EtOH:MeCN:H₂O/3:1:1, vortexed and the supernatant is then added to the first supernatant. The combined supernatants, containing the oligoribonucleotide, are dried to a white powder.

The method of synthesis used for normal RNA including certain decoy nucleic acid molecules and enzymatic nucleic acid molecules follows the procedure as described in Usman *et al.*, 1987, *J. Am. Chem. Soc.*, 109, 7845; Scaringe *et al.*, 1990, *Nucleic Acids Res.*, 18, 5433; and Wincott *et al.*, 1995, *Nucleic Acids Res.* 23, 2677-2684 Wincott *et al.*, 1997, *Methods Mol. Bio.*, 74, 59, and makes use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. In a non-limiting example, small scale syntheses are conducted on a 394 Applied Biosystems, Inc. synthesizer using a 0.2 µmol scale protocol with a 7.5 min coupling step for alkylsilyl protected nucleotides and a 2.5 min coupling step for 2'-O-methylated nucleotides. **Table II** outlines the amounts and the contact times of the reagents used in the synthesis cycle. Alternatively, syntheses at the 0.2 µmol scale can be done on a 96-well plate synthesizer, such as the instrument produced by Protogene (Palo Alto, CA) with minimal modification to the cycle. A 33-fold excess (60 µL of 0.11 M = 6.6 µmol) of 2'-O-methyl phosphoramidite and a 75-fold excess of S-ethyl tetrazole (60 µL of 0.25 M = 15 µmol) can be used in each coupling cycle of 2'-O-methyl residues relative to polymer-bound 5'-hydroxyl. A 66-fold excess (120 µL of 0.11 M = 13.2 µmol) of alkylsilyl (ribo) protected phosphoramidite and a 150-fold excess of S-ethyl tetrazole (120 µL of 0.25 M = 30 µmol) can be used in each coupling cycle of ribo residues relative to polymer-bound 5'-hydroxyl. Average coupling yields on the 394 Applied Biosystems, Inc. synthesizer, determined by colorimetric quantitation of the trityl fractions, are typically 97.5-99%. Other oligonucleotide synthesis reagents for the 394 Applied Biosystems, Inc. synthesizer include the following: detritylation

solution is 3% TCA in methylene chloride (ABI); capping is performed with 16% *N*-methylimidazole in THF (ABI) and 10% acetic anhydride/10% 2,6-lutidine in THF (ABI); oxidation solution is 16.9 mM I₂, 49 mM pyridine, 9% water in THF (PERSEPTIVE™). Burdick & Jackson Synthesis Grade acetonitrile is used directly from the reagent bottle. S-Ethyltetrazole solution (0.25 M in acetonitrile) is made up from the solid obtained from American International Chemical, Inc. Alternately, for the introduction of phosphorothioate linkages, Beaucage reagent (3H-1,2-Benzodithiol-3-one 1,1-dioxide) 0.05 M in acetonitrile is used.

Deprotection of the RNA is performed using either a two-pot or one-pot protocol. For the two-pot protocol, the polymer-bound trityl-on oligoribonucleotide is transferred to a 4 mL glass screw top vial and suspended in a solution of 40% aq. methylamine (1 mL) at 65 °C for 10 min. After cooling to -20 °C, the supernatant is removed from the polymer support. The support is washed three times with 1.0 mL of EtOH:MeCN:H₂O/3:1:1, vortexed and the supernatant is then added to the first supernatant. The combined supernatants, containing the oligoribonucleotide, are dried to a white powder. The base deprotected oligoribonucleotide is resuspended in anhydrous TEA/HF/NMP solution (300 µL of a solution of 1.5 mL *N*-methylpyrrolidinone, 750 µL TEA and 1 mL TEA•3HF to provide a 1.4 M HF concentration) and heated to 65 °C. After 1.5 h, the oligomer is quenched with 1.5 M NH₄HCO₃.

Alternatively, for the one-pot protocol, the polymer-bound trityl-on oligoribonucleotide is transferred to a 4 mL glass screw top vial and suspended in a solution of 33% ethanolic methylamine/DMSO: 1/1 (0.8 mL) at 65 °C for 15 min. The vial is brought to r.t. TEA•3HF (0.1 mL) is added and the vial is heated at 65 °C for 15 min. The sample is cooled at -20 °C and then quenched with 1.5 M NH₄HCO₃.

For purification of the trityl-on oligomers, the quenched NH₄HCO₃ solution is loaded onto a C-18 containing cartridge that had been prewashed with acetonitrile followed by 50 mM TEAA. After washing the loaded cartridge with water, the RNA is detritylated with 0.5% TFA for 13 min. The cartridge is then washed again with water, salt exchanged with 1 M NaCl and washed with water again. The oligonucleotide is then eluted with 30% acetonitrile.

Inactive hammerhead ribozymes or binding attenuated control (BAC) oligonucleotides are synthesized by substituting a U for G₅ and a U for A₁₄ (numbering from Hertel, K. J., *et al.*, 1992, *Nucleic Acids Res.*, 20, 3252). Similarly, one or more nucleotide substitutions can be introduced in other nucleic acid decoy molecules to inactivate the molecule and such molecules can serve as a negative control.

The average stepwise coupling yields are typically >98% (Wincott *et al.*, 1995 *Nucleic Acids Res.* 23, 2677-2684). Those of ordinary skill in the art will recognize that the scale of synthesis can be adapted to be larger or smaller than the example described above including but not limited to 96-well format, all that is important is the ratio of chemicals used in the reaction.

Alternatively, the nucleic acid molecules of the present invention can be synthesized separately and joined together post-synthetically, for example, by ligation (Moore *et al.*, 1992, *Science* 256, 9923; Draper *et al.*, International PCT publication No. WO 93/23569; Shabarova *et al.*, 1991, *Nucleic Acids Research* 19, 4247; Bellon *et al.*, 1997, *Nucleosides & Nucleotides*, 16, 951; Bellon *et al.*, 1997, *Bioconjugate Chem.* 8, 204).

The nucleic acid molecules of the present invention can be modified extensively to enhance stability by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-fluoro, 2'-O-methyl, 2'-H (for a review see Usman and Cedergren, 1992, *TIBS* 17, 34; Usman *et al.*, 1994, *Nucleic Acids Symp. Ser.* 31, 163). Ribozymes can be purified by gel electrophoresis using general methods or can be purified by high pressure liquid chromatography (HPLC; see Wincott *et al.*, *supra*, the totality of which is hereby incorporated herein by reference) and re-suspended in water.

The sequences of the nucleic acid molecules that are chemically synthesized, useful in this study, are shown in Tables XI, XV, XX, XXI, XXII and XXIII. The nucleic acid sequences listed in Tables IV-XI, XIV-XV and XVIII-XXIII can be formed of ribonucleotides or other nucleotides or non-nucleotides. Such nucleic acid sequences are equivalent to the sequences described specifically in the Tables.

Optimizing Activity of the nucleic acid molecule of the invention

Chemically synthesizing nucleic acid molecules with modifications (base, sugar and/or phosphate) can prevent their degradation by serum ribonucleases, which can increase their potency (see *e.g.*, Eckstein *et al.*, International Publication No. WO 92/07065; Perrault *et al.*, 1990 *Nature* 344, 565; Pieken *et al.*, 1991, *Science* 253, 314; Usman and Cedergren, 1992, *Trends in Biochem. Sci.* 17, 334; Usman *et al.*, International Publication No. WO 93/15187; and Rossi *et al.*, International Publication No. WO 91/03162; Sproat, US Patent No. 5,334,711; Gold *et al.*, US 6,300,074; and Burgin *et al.*, *supra*; all of which are incorporated by reference herein). All of the above references describe various chemical modifications that can be made to the base, phosphate and/or sugar moieties of the nucleic acid molecules described herein. Modifications that enhance their efficacy in cells, and removal of bases from nucleic acid molecules to shorten oligonucleotide synthesis times and reduce chemical requirements are desired.

There are several examples in the art describing sugar, base and phosphate modifications that can be introduced into nucleic acid molecules with significant enhancement in their nuclease stability and efficacy. For example, oligonucleotides are modified to enhance stability and/or enhance biological activity by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-fluoro, 2'-O-methyl, 2'-H, nucleotide base modifications (for a review see Usman and Cedergren, 1992, *TIBS*, 17, 34; Usman *et al.*, 1994, *Nucleic Acids Symp. Ser.* 31, 163; Burgin *et al.*, 1996, *Biochemistry*, 35, 14090). Sugar modification of nucleic acid molecules have been extensively described in the art (see Eckstein *et al.*, *International Publication* PCT No. WO 92/07065; Perrault *et al.* *Nature*, 1990, 344, 565-568; Pieken *et al.* *Science*, 1991, 253, 314-317; Usman and Cedergren, *Trends in Biochem. Sci.*, 1992, 17, 334-339; Usman *et al.* *International Publication* PCT No. WO 93/15187; Sproat, *US Patent* No. 5,334,711 and Beigelman *et al.*, 1995, *J. Biol. Chem.*, 270, 25702; Beigelman *et al.*, *International PCT publication* No. WO 97/26270; Beigelman *et al.*, *US Patent* No. 5,716,824; Usman *et al.*, *US patent* No. 5,627,053; Woolf *et al.*, *International PCT Publication* No. WO 98/13526; Thompson *et al.*, *USSN* 60/082,404 which was filed on April 20, 1998; Karpeisky *et al.*, 1998, *Tetrahedron Lett.*, 39, 1131; Earnshaw and Gait, 1998, *Biopolymers (Nucleic Acid Sciences)*, 48, 39-55; Verma and Eckstein, 1998, *Annu. Rev. Biochem.*, 67, 99-134; and Burlina *et al.*, 1997, *Bioorg. Med. Chem.*, 5, 1999-2010; all of the references are hereby incorporated in their totality by reference herein). Such publications describe general methods and strategies to determine the location of incorporation of sugar, base and/or phosphate modifications and the like into ribozymes without modulating catalysis, and are incorporated by reference herein. In view of such teachings, similar modifications can be used as described herein to modify the nucleic acid molecules of the instant invention.

While chemical modification of oligonucleotide internucleotide linkages with phosphorothioate, phosphorothioate, and/or 5'-methylphosphonate linkages improves stability, excessive modifications can cause some toxicity. Therefore, when designing nucleic acid molecules, the amount of these internucleotide linkages should be minimized. The reduction in the concentration of these linkages should lower toxicity, resulting in increased efficacy and higher specificity of these molecules.

Nucleic acid molecules having chemical modifications that maintain or enhance activity are provided. Such a nucleic acid is also generally more resistant to nucleases than an unmodified nucleic acid. Accordingly, the *in vitro* and/or *in vivo* activity should not be significantly lowered. In cases in which modulation is the goal, therapeutic nucleic acid molecules delivered exogenously should optimally be stable within cells until translation of the target RNA has been modulated long enough to reduce the levels of the undesirable protein. This period of time varies between hours to days depending upon the disease state.

Improvements in the chemical synthesis of RNA and DNA (Wincott *et al.*, 1995 *Nucleic Acids Res.* 23, 2677; Caruthers *et al.*, 1992, *Methods in Enzymology* 211,3-19 (incorporated by reference herein)) have expanded the ability to modify nucleic acid molecules by introducing nucleotide modifications to enhance their nuclease stability, as described above.

In one embodiment, nucleic acid molecules of the invention include one or more G-clamp nucleotides. A G-clamp nucleotide is a modified cytosine analog wherein the modifications confer the ability to hydrogen bond both Watson-Crick and Hoogsteen faces of a complementary guanine within a duplex, see for example Lin and Matteucci, 1998, *J. Am. Chem. Soc.*, 120, 8531-8532. A single G-clamp analog substitution within an oligonucleotide can result in substantially enhanced helical thermal stability and mismatch discrimination when hybridized to complementary oligonucleotides. The inclusion of such nucleotides in nucleic acid molecules of the invention results in both enhanced affinity and specificity to nucleic acid targets. In another embodiment, nucleic acid molecules of the invention include one or more LNA "locked nucleic acid" nucleotides such as a 2', 4'-C methylene bicyclo nucleotide (see for example Wengel *et al.*, International PCT Publication No. WO 00/66604 and WO 99/14226).

In another embodiment, the invention features conjugates and/or complexes of nucleic acid molecules targeting HBV or HCV. Such conjugates and/or complexes can be used to facilitate delivery of molecules into a biological system, such as a cell. The conjugates and complexes provided by the instant invention can impart therapeutic activity by transferring therapeutic compounds across cellular membranes, altering the pharmacokinetics, and/or modulating the localization of nucleic acid molecules of the invention. The present invention encompasses the design and synthesis of novel conjugates and complexes for the delivery of molecules, including, but not limited to, small molecules, lipids, phospholipids, nucleosides, nucleotides, nucleic acids, antibodies, toxins, negatively charged polymers and other polymers, for example proteins, peptides, hormones, carbohydrates, polyethylene glycols, or polyamines, across cellular membranes. In general, the transporters described are designed to be used either individually or as part of a multi-component system, with or without degradable linkers. These compounds are expected to improve delivery and/or localization of nucleic acid molecules of the invention into a number of cell types originating from different tissues, in the presence or absence of serum (see Sullenger and Cech, US 5,854,038). Conjugates of the molecules described herein can be attached to biologically active molecules via linkers that are biodegradable, such as biodegradable nucleic acid linker molecules.

The term "biodegradable nucleic acid linker molecule" as used herein, refers to a nucleic acid molecule that is designed as a biodegradable linker to connect one molecule to another molecule, for example, a biologically active molecule. The stability of the

biodegradable nucleic acid linker molecule can be modulated by using various combinations of ribonucleotides, deoxyribonucleotides, and chemically modified nucleotides, for example, 2'-O-methyl, 2'-fluoro, 2'-amino, 2'-O-amino, 2'-C-allyl, 2'-O-allyl, and other 2'-modified or base modified nucleotides. The biodegradable nucleic acid linker molecule can be a dimer, trimer, tetramer or longer nucleic acid molecule, for example, an oligonucleotide of about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length, or can comprise a single nucleotide with a phosphorus-based linkage, for example, a phosphoramidate or phosphodiester linkage. The biodegradable nucleic acid linker molecule can also comprise nucleic acid backbone, nucleic acid sugar, or nucleic acid base modifications.

The term "biodegradable" as used herein, refers to degradation in a biological system, for example enzymatic degradation or chemical degradation.

The term "biologically active molecule" as used herein, refers to compounds or molecules that are capable of eliciting or modifying a biological response in a system. Non-limiting examples of biologically active molecules contemplated by the instant invention include therapeutically active molecules such as antibodies, hormones, antivirals, peptides, proteins, chemotherapeutics, small molecules, vitamins, co-factors, nucleosides, nucleotides, oligonucleotides, enzymatic nucleic acids, antisense nucleic acids, triplex forming oligonucleotides, 2,5-A chimeras, siRNA, dsRNA, allozymes, aptamers, decoys and analogs thereof. Biologically active molecules of the invention also include molecules capable of modulating the pharmacokinetics and/or pharmacodynamics of other biologically active molecules, for example, lipids and polymers such as polyamines, polyamides, polyethylene glycol and other polyethers.

The term "phospholipid" as used herein, refers to a hydrophobic molecule comprising at least one phosphorus group. For example, a phospholipid can comprise a phosphorus-containing group and saturated or unsaturated alkyl group, optionally substituted with OH, COOH, oxo, amine, or substituted or unsubstituted aryl groups.

Therapeutic nucleic acid molecules (*e.g.*, decoy nucleic acid molecules) delivered exogenously optimally are stable within cells until reverse transcription of the pregenomic RNA has been modulated long enough to reduce the levels of HBV or HCV DNA. The nucleic acid molecules are resistant to nucleases in order to function as effective intracellular therapeutic agents. Improvements in the chemical synthesis of nucleic acid molecules described in the instant invention and in the art have expanded the ability to modify nucleic acid molecules by introducing nucleotide modifications to enhance their nuclease stability as described above.

In yet another embodiment, nucleic acid molecules having chemical modifications that maintain or enhance enzymatic activity are provided. Such nucleic acids are also generally more resistant to nucleases than unmodified nucleic acids. Thus, *in vitro* and/or *in vivo* the activity should not be significantly lowered. As exemplified herein, such nucleic acid molecules are useful *in vitro* and/or *in vivo* even if activity over all is reduced 10 fold (Burgin *et al.*, 1996, *Biochemistry*, 35, 14090).

Use of the nucleic acid-based molecules of the invention will lead to better treatment of the disease progression by affording the possibility of combination therapies (e.g., multiple antisense, nucleic acid decoy, or nucleic acid aptamer molecules targeted to different genes; nucleic acid molecules coupled with known small molecule modulators or; or intermittent treatment with combinations of molecules (including different motifs) and/or other chemical or biological molecules). The treatment of patients with nucleic acid molecules may also include combinations of different types of nucleic acid molecules.

In another aspect the nucleic acid molecules comprise a 5' and/or a 3'-cap structure.

By "cap structure" is meant chemical modifications, which have been incorporated at either terminus of the oligonucleotide (see, for example, Wincott *et al.*, WO 97/26270, incorporated by reference herein). These terminal modifications protect the nucleic acid molecule from exonuclease degradation, and may help in delivery and/or localization within a cell. The cap may be present at the 5'-terminus (5'-cap) or at the 3'-terminal (3'-cap) or may be present on both termini. In non-limiting examples: the 5'-cap is selected from the group comprising inverted abasic residue (moiety); 4',5'-methylene nucleotide; 1-(beta-D-erythrofuranosyl) nucleotide; 4'-thio nucleotide; carbocyclic nucleotide; 1,5-anhydrohexitol nucleotide; L-nucleotides; alpha-nucleotides; modified base nucleotide; phosphorodithioate linkage; *threo*-pentofuranosyl nucleotide; acyclic 3',4'-seco nucleotide; acyclic 3,4-dihydroxybutyl nucleotide; acyclic 3,5-dihydroxypentyl nucleotide, 3'-3'-inverted nucleotide moiety; 3'-3'-inverted abasic moiety; 3'-2'-inverted nucleotide moiety; 3'-2'-inverted abasic moiety; 1,4-butanediol phosphate; 3'-phosphoramidate; hexylphosphate; aminohexyl phosphate; 3'-phosphate; 3'-phosphorothioate; phosphorodithioate; or bridging or non-bridging methylphosphonate moiety (for more details, see Wincott *et al.*, International PCT publication No. WO 97/26270, incorporated by reference herein).

In yet another preferred embodiment, the 3'-cap is selected from a group comprising, 4',5'-methylene nucleotide; 1-(beta-D-erythrofuranosyl) nucleotide; 4'-thio nucleotide, carbocyclic nucleotide; 5'-amino-alkyl phosphate; 1,3-diamino-2-propyl phosphate; 3-aminopropyl phosphate; 6-aminoethyl phosphate; 1,2-aminododecyl phosphate; hydroxypropyl phosphate; 1,5-anhydrohexitol nucleotide; L-nucleotide; alpha-nucleotide; modified base nucleotide; phosphorodithioate; *threo*-pentofuranosyl nucleotide; acyclic 3',4'-

seco nucleotide; 3,4-dihydroxybutyl nucleotide; 3,5-dihydroxypentyl nucleotide, 5'-5'-inverted nucleotide moiety; 5'-5'-inverted abasic moiety; 5'-phosphoramidate; 5'-phosphorothioate; 1,4-butanediol phosphate; 5'-amino; bridging and/or non-bridging 5'-phosphoramidate, phosphorothioate and/or phosphorodithioate, bridging or non bridging methylphosphonate and 5'-mercapto moieties (for more details see Beaucage and Iyer, 1993, *Tetrahedron* 49, 1925; incorporated by reference herein).

By the term "non-nucleotide" is meant any group or compound which can be incorporated into a nucleic acid chain in the place of one or more nucleotide units, including either sugar and/or phosphate substitutions, and allows the remaining bases to exhibit their enzymatic activity. The group or compound is abasic in that it does not contain a commonly recognized nucleotide base, such as adenosine, guanine, cytosine, uracil or thymine.

The term "alkyl" as used herein refers to a saturated aliphatic hydrocarbon, including straight-chain, branched-chain "isoalkyl", and cyclic alkyl groups. The term "alkyl" also comprises alkoxy, alkyl-thio, alkyl-thio-alkyl, alkoxyalkyl, alkylamino, alkenyl, alkynyl, alkoxy, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, C1-C6 hydrocarbyl, aryl or substituted aryl groups. Preferably, the alkyl group has 1 to 12 carbons. More preferably it is a lower alkyl of from about 1 to 7 carbons, more preferably about 1 to 4 carbons. The alkyl group can be substituted or unsubstituted. When substituted the substituted group(s) preferably comprise hydroxy, oxy, thio, amino, nitro, cyano, alkoxy, alkyl-thio, alkyl-thio-alkyl, alkoxyalkyl, alkylamino, silyl, alkenyl, alkynyl, alkoxy, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, C1-C6 hydrocarbyl, aryl or substituted aryl groups. The term "alkyl" also includes alkenyl groups containing at least one carbon-carbon double bond, including straight-chain, branched-chain, and cyclic groups. Preferably, the alkenyl group has about 2 to 12 carbons. More preferably it is a lower alkenyl of from about 2 to 7 carbons, more preferably about 2 to 4 carbons. The alkenyl group can be substituted or unsubstituted. When substituted the substituted group(s) preferably comprise hydroxy, oxy, thio, amino, nitro, cyano, alkoxy, alkyl-thio, alkyl-thio-alkyl, alkoxyalkyl, alkylamino, silyl, alkenyl, alkynyl, alkoxy, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, C1-C6 hydrocarbyl, aryl or substituted aryl groups. The term "alkyl" also includes alkynyl groups containing at least one carbon-carbon triple bond, including straight-chain, branched-chain, and cyclic groups. Preferably, the alkynyl group has about 2 to 12 carbons. More preferably it is a lower alkynyl of from about 2 to 7 carbons, more preferably about 2 to 4 carbons. The alkynyl group can be substituted or unsubstituted. When substituted the substituted group(s) preferably comprise hydroxy, oxy, thio, amino, nitro, cyano, alkoxy, alkyl-thio, alkyl-thio-alkyl, alkoxyalkyl, alkylamino, silyl, alkenyl, alkynyl, alkoxy, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, C1-C6 hydrocarbyl, aryl or substituted aryl groups. Alkyl groups or moieties of

the invention can also include aryl, alkylaryl, carbocyclic aryl, heterocyclic aryl, amide and ester groups. The preferred substituent(s) of aryl groups are halogen, trihalomethyl, hydroxyl, SH, OH, cyano, alkoxy, alkyl, alkenyl, alkynyl, and amino groups. An "alkylaryl" group refers to an alkyl group (as described above) covalently joined to an aryl group (as described above). Carbocyclic aryl groups are groups wherein the ring atoms on the aromatic ring are all carbon atoms. The carbon atoms are optionally substituted. Heterocyclic aryl groups are groups having from about 1 to 3 heteroatoms as ring atoms in the aromatic ring and the remainder of the ring atoms are carbon atoms. Suitable heteroatoms include oxygen, sulfur, and nitrogen, and include furanyl, thienyl, pyridyl, pyrrolyl, N-lower alkyl pyrrolo, pyrimidyl, pyrazinyl, imidazolyl and the like, all optionally substituted. An "amide" refers to an $-C(O)-NH-R$, where R is either alkyl, aryl, alkylaryl or hydrogen. An "ester" refers to an $-C(O)-OR'$, where R is either alkyl, aryl, alkylaryl or hydrogen.

The term "alkoxyalkyl" as used herein refers to an alkyl-O-alkyl ether, for example methoxyethyl or ethoxymethyl.

The term "alkyl-thio-alkyl" as used herein refers to an alkyl-S-alkyl thioether, for example methylthiomethyl or methylthioethyl.

The term "amination" as used herein refers to a process in which an amino group or substituted amine is introduced into an organic molecule.

The term "exocyclic amine protecting moiety" as used herein refers to a nucleobase amino protecting group compatible with oligonucleotide synthesis, for example an acyl or amide group.

The term "alkenyl" as used herein refers to a straight or branched hydrocarbon of a designed number of carbon atoms containing at least one carbon-carbon double bond. Examples of "alkenyl" include vinyl, allyl, and 2-methyl-3-heptene.

The term "alkoxy" as used herein refers to an alkyl group of indicated number of carbon atoms attached to the parent molecular moiety through an oxygen bridge. Examples of alkoxy groups include, for example, methoxy, ethoxy, propoxy and isopropoxy.

The term "alkynyl" as used herein refers to a straight or branched hydrocarbon of a designed number of carbon atoms containing at least one carbon-carbon triple bond. Examples of "alkynyl" include propargyl, propyne, and 3-hexyne.

The term "aryl" as used herein refers to an aromatic hydrocarbon ring system containing at least one aromatic ring. The aromatic ring can optionally be fused or otherwise attached to other aromatic hydrocarbon rings or non-aromatic hydrocarbon rings. Examples

of aryl groups include, for example, phenyl, naphthyl, 1,2,3,4-tetrahydronaphthalene and biphenyl. Preferred examples of aryl groups include phenyl and naphthyl.

The term "cycloalkenyl" as used herein refers to a C3-C8 cyclic hydrocarbon containing at least one carbon-carbon double bond. Examples of cycloalkenyl include cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclopentadiene, cyclohexenyl, 1,3-cyclohexadiene, cycloheptenyl, cycloheptatrienyl, and cyclooctenyl.

The term "cycloalkyl" as used herein refers to a C3-C8 cyclic hydrocarbon. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

The term "cycloalkylalkyl," as used herein, refers to a C3-C7 cycloalkyl group attached to the parent molecular moiety through an alkyl group, as defined above. Examples of cycloalkylalkyl groups include cyclopropylmethyl and cyclopentylethyl.

The terms "halogen" or "halo" as used herein refers to indicate fluorine, chlorine, bromine, and iodine.

The term "heterocycloalkyl," as used herein refers to a non-aromatic ring system containing at least one heteroatom selected from nitrogen, oxygen, and sulfur. The heterocycloalkyl ring can be optionally fused to or otherwise attached to other heterocycloalkyl rings and/or non-aromatic hydrocarbon rings. Preferred heterocycloalkyl groups have from 3 to 7 members. Examples of heterocycloalkyl groups include, for example, piperazine, morpholine, piperidine, tetrahydrofuran, pyrrolidine, and pyrazole. Preferred heterocycloalkyl groups include piperidinyl, piperazinyl, morpholinyl, and pyrrolidinyl.

The term "heteroaryl" as used herein refers to an aromatic ring system containing at least one heteroatom selected from nitrogen, oxygen, and sulfur. The heteroaryl ring can be fused or otherwise attached to one or more heteroaryl rings, aromatic or non-aromatic hydrocarbon rings or heterocycloalkyl rings. Examples of heteroaryl groups include, for example, pyridine, furan, thiophene, 5,6,7,8-tetrahydroisoquinoline and pyrimidine. Preferred examples of heteroaryl groups include thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, benzimidazolyl, furanyl, benzofuranyl, thiazolyl, benzothiazolyl, isoxazolyl, oxadiazolyl, isothiazolyl, benzisothiazolyl, triazolyl, tetrazolyl, pyrrolyl, indolyl, pyrazolyl, and benzopyrazolyl.

The term "C1-C6 hydrocarbyl" as used herein refers to straight, branched, or cyclic alkyl groups having 1-6 carbon atoms, optionally containing one or more carbon-carbon double or triple bonds. Examples of hydrocarbyl groups include, for example, methyl, ethyl,

propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, pentyl, 2-pentyl, isopentyl, neopentyl, hexyl, 2-hexyl, 3-hexyl, 3-methylpentyl, vinyl, 2-pentene, cyclopropylmethyl, cyclopropyl, cyclohexylmethyl, cyclohexyl and propargyl. When reference is made herein to C1-C6 hydrocarbonyl containing one or two double or triple bonds it is understood that at least two carbons are present in the alkyl for one double or triple bond, and at least four carbons for two double or triple bonds.

The term "nucleotide" as used herein refers to a heterocyclic nitrogenous base in N-glycosidic linkage with a phosphorylated sugar. Nucleotides are recognized in the art to include natural bases (standard), and modified bases well known in the art. Such bases are generally located at the 1' position of a nucleotide sugar moiety. Nucleotides generally comprise a base, sugar and a phosphate group. The nucleotides can be unmodified or modified at the sugar, phosphate and/or base moiety, (also referred to interchangeably as nucleotide analogs, modified nucleotides, non-natural nucleotides, non-standard nucleotides and other; see for example, Usman and McSwiggen, *supra*; Eckstein *et al.*, International PCT Publication No. WO 92/07065; Usman *et al.*, International PCT Publication No. WO 93/15187; Uhlman & Peyman, *supra* all are hereby incorporated by reference herein. There are several examples of modified nucleic acid bases known in the art as summarized by Limbach *et al.*, 1994, Nucleic Acids Res. 22, 2183. Some of the non-limiting examples of chemically modified and other natural nucleic acid bases that can be introduced into nucleic acids include, for example, inosine, purine, pyridin-4-one, pyridin-2-one, phenyl, pseudouracil, 2, 4, 6-trimethoxy benzene, 3-methyl uracil, dihydrouridine, naphthyl, aminophenyl, 5-alkylcytidines (*e.g.*, 5-methylcytidine), 5-alkyluridines (*e.g.*, ribothymidine), 5-halouridine (*e.g.*, 5-bromouridine) or 6-azapyrimidines or 6-alkylpyrimidines (*e.g.* 6-methyluridine), propyne, quesosine, 2-thiouridine, 4-thiouridine, wybutosine, wybutoxosine, 4-acetylcytidine, 5-(carboxyhydroxymethyl)uridine, 5'-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluridine, beta-D-galactosylqueosine, 1-methyladenosine, 1-methylinosine, 2,2-dimethylguanosine, 3-methylcytidine, 2-methyladenosine, 2-methylguanosine, N6-methyladenosine, 7-methylguanosine, 5-methoxyaminomethyl-2-thiouridine, 5-methylaminomethyluridine, 5-methylcarbonylmethyluridine, 5-methoxyuridine, 5-methyl-2-thiouridine, 2-methylthio-N6-isopentenyladenosine, beta-D-mannosylqueosine, uridine-5-oxyacetic acid, 2-thiocytidine, threonine derivatives and others (Burgin *et al.*, 1996, Biochemistry, 35, 14090; Uhlman & Peyman, *supra*). By "modified bases" in this aspect is meant nucleotide bases other than adenine, guanine, cytosine and uracil at 1' position or their equivalents; such bases can be used at any position, for example, within the catalytic core of an enzymatic nucleic acid molecule and/or in the substrate-binding regions of the nucleic acid molecule.

The term "nucleoside" as used herein refers to a heterocyclic nitrogenous base in N-glycosidic linkage with a sugar. Nucleosides are recognized in the art to include natural bases (standard), and modified bases well known in the art. Such bases are generally located at the 1' position of a nucleoside sugar moiety. Nucleosides generally comprise a base and sugar group. The nucleosides can be unmodified or modified at the sugar, and/or base moiety (also referred to interchangeably as nucleoside analogs, modified nucleosides, non-natural nucleosides, non-standard nucleosides and other; see for example, Usman and McSwiggen, *supra*; Eckstein *et al.*, International PCT Publication No. WO 92/07065; Usman *et al.*, International PCT Publication No. WO 93/15187; Uhlman & Peyman, *supra* all are hereby incorporated by reference herein). There are several examples of modified nucleic acid bases known in the art as summarized by Limbach *et al.*, 1994, *Nucleic Acids Res.* 22, 2183. Some of the non-limiting examples of chemically modified and other natural nucleic acid bases that can be introduced into nucleic acids include, inosine, purine, pyridin-4-one, pyridin-2-one, phenyl, pseudouracil, 2, 4, 6-trimethoxy benzene, 3-methyl uracil, dihydrouridine, naphthyl, aminophenyl, 5-alkylcytidines (*e.g.*, 5-methylcytidine), 5-alkyluridines (*e.g.*, ribothymidine), 5-halouridine (*e.g.*, 5-bromouridine) or 6-azapyrimidines or 6-alkylpyrimidines (*e.g.* 6-methyluridine), propyne, queosine, 2-thiouridine, 4-thiouridine, wybutosine, wybutoxosine, 4-acetylcytidine, 5-(carboxyhydroxymethyl)uridine, 5'-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluridine, beta-D-galactosylqueosine, 1-methyladenosine, 1-methylinosine, 2,2-dimethylguanosine, 3-methylcytidine, 2-methyladenosine, 2-methylguanosine, N6-methyladenosine, 7-methylguanosine, 5-methoxyaminomethyl-2-thiouridine, 5-methylaminomethyluridine, 5-methylcarbonylmethyluridine, 5-methoxyuridine, 5-methyl-2-thiouridine, 2-methylthio-N6-isopentenyladenosine, beta-D-mannosylqueosine, uridine-5-oxyacetic acid, 2-thiocytidine, threonine derivatives and others (Burgin *et al.*, 1996, *Biochemistry*, 35, 14090; Uhlman & Peyman, *supra*). By "modified bases" in this aspect is meant nucleoside bases other than adenine, guanine, cytosine and uracil at 1' position or their equivalents; such bases can be used at any position, for example, within the catalytic core of an enzymatic nucleic acid molecule and/or in the substrate-binding regions of the nucleic acid molecule.

In one embodiment, the invention features modified nucleic acid molecules with phosphate backbone modifications comprising one or more phosphorothioate, phosphorodithioate, methylphosphonate, morpholino, amidate carbamate, carboxymethyl, acetamidate, polyamide, sulfonate, sulfonamide, sulfamate, formacetal, thioformacetal, and/or alkylsilyl, substitutions. For a review of oligonucleotide backbone modifications see Hunziker and Leumann, 1995, *Nucleic Acid Analogues: Synthesis and Properties*, in *Modern Synthetic Methods*, VCH, 331-417, and Mesmaeker *et al.*, 1994, *Novel Backbone Replacements for Oligonucleotides*, in *Carbohydrate Modifications in Antisense Research*, ACS, 24-39. These references are hereby incorporated by reference herein.

The term "abasic" as used herein refers to sugar moieties lacking a base or having other chemical groups in place of a base at the 1' position, for example a 3',3'-linked or 5',5'-linked deoxyabasic ribose derivative (for more details see Wincott *et al.*, International PCT publication No. WO 97/26270).

The term "unmodified nucleoside" as used herein refers to one of the bases adenine, cytosine, guanine, thymine, uracil joined to the 1' carbon of β -D-ribo-furanose.

The term "modified nucleoside" as used herein refers to any nucleotide base which contains a modification in the chemical structure of an unmodified nucleotide base, sugar and/or phosphate.

In connection with 2'-modified nucleotides as described for the present invention, by "amino" is meant 2'-NH₂ or 2'-O- NH₂, which can be modified or unmodified. Such modified groups are described, for example, in Eckstein *et al.*, U.S. Patent 5,672,695 and Matulic-Adamic *et al.*, WO 98/28317, respectively, which are both incorporated by reference in their entireties.

Various modifications to nucleic acid (*e.g.*, enzymatic nucleic acid, antisense, decoy, aptamer, siRNA, triplex oligonucleotides, 2,5-A oligonucleotides and other nucleic acid molecules) structure can be made to enhance the utility of these molecules. For example, such modifications can enhance shelf life, half-life *in vitro*, stability, and ease of introduction of such oligonucleotides to the target site, including *e.g.*, enhancing penetration of cellular membranes and conferring the ability to recognize and bind to targeted cells.

Use of these molecules can lead to better treatment of the disease progression by affording the possibility of combination therapies (*e.g.*, multiple nucleic acid molecules targeted to different genes, nucleic acid molecules coupled with known small molecule inhibitors, or intermittent treatment with combinations of nucleic acid molecules (including different nucleic acid molecule motifs) and/or other chemical or biological molecules). The treatment of patients with nucleic acid molecules can also include combinations of different types of nucleic acid molecules. Therapies can be devised which include a mixture of enzymatic nucleic acid molecules (including different enzymatic nucleic acid molecule motifs), antisense, decoy, aptamer and/or 2-5A chimera molecules to one or more targets to alleviate symptoms of a disease.

Administration of Nucleic Acid Molecules

Methods for the delivery of nucleic acid molecules are described in Akhtar *et al.*, 1992, *Trends Cell Bio.*, 2, 139; *Delivery Strategies for Antisense Oligonucleotide Therapeutics*, ed. Akhtar, 1995, Maurer *et al.*, 1999, *Mol. Membr. Biol.*, 16, 129-140; Hofland and Huang,

1999, *Handb. Exp. Pharmacol.*, 137, 165-192; and Lee *et al.*, 2000, *ACS Symp. Ser.*, 752, 184-192, Sullivan *et al.*, PCT WO 94/02595, further describes the general methods for delivery of enzymatic nucleic acid molecules. These protocols can be utilized for the delivery of virtually any nucleic acid molecule. Nucleic acid molecules can be administered to cells by a variety of methods known to those of skill in the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres, or by proteinaceous vectors (O'Hare and Normand, International PCT Publication No. WO 00/53722). Alternatively, the nucleic acid/vehicle combination is locally delivered by direct injection or by use of an infusion pump. Direct injection of the nucleic acid molecules of the invention, whether subcutaneous, intramuscular, or intradermal, can take place using standard needle and syringe methodologies, or by needle-free technologies such as those described in Conry *et al.*, 1999, *Clin. Cancer Res.*, 5, 2330-2337 and Barry *et al.*, International PCT Publication No. WO 99/31262. The molecules of the instant invention can be used as pharmaceutical agents. Pharmaceutical agents prevent, modulate the occurrence, or treat (alleviate a symptom to some extent, preferably all of the symptoms) of a disease state in a patient.

Thus, the invention features a pharmaceutical composition comprising one or more nucleic acid(s) of the invention in an acceptable carrier, such as a stabilizer, buffer, and the like. The negatively charged polynucleotides of the invention can be administered (*e.g.*, RNA, DNA or protein) and introduced into a patient by any standard means, with or without stabilizers, buffers, and the like, to form a pharmaceutical composition. When it is desired to use a liposome delivery mechanism, standard protocols for formation of liposomes can be followed. The compositions of the present invention may also be formulated and used as tablets, capsules or elixirs for oral administration, suppositories for rectal administration, sterile solutions, suspensions for injectable administration, and the other compositions known in the art.

The present invention also includes pharmaceutically acceptable formulations of the compounds described. These formulations include salts of the above compounds, *e.g.*, acid addition salts, for example, salts of hydrochloric, hydrobromic, acetic acid, and benzene sulfonic acid.

A pharmacological composition or formulation refers to a composition or formulation in a form suitable for administration, *e.g.*, systemic administration, into a cell or patient, including for example a human. Suitable forms, in part, depend upon the use or the route of entry, for example oral, transdermal, or by injection. Such forms should not prevent the composition or formulation from reaching a target cell (*i.e.*, a cell to which the negatively

charged nucleic acid is desirable for delivery). For example, pharmacological compositions injected into the blood stream should be soluble. Other factors are known in the art, and include considerations such as toxicity and forms that prevent the composition or formulation from exerting its effect.

By "systemic administration" is meant *in vivo* systemic absorption or accumulation of drugs in the blood stream followed by distribution throughout the entire body. Administration routes which lead to systemic absorption include, without limitation: intravenous, subcutaneous, intraperitoneal, inhalation, oral, intrapulmonary and intramuscular. Each of these administration routes expose the desired negatively charged polymers, *e.g.*, nucleic acids, to an accessible diseased tissue. The rate of entry of a drug into the circulation has been shown to be a function of molecular weight or size. The use of a liposome or other drug carrier comprising the compounds of the instant invention can potentially localize the drug, for example, in certain tissue types, such as the tissues of the reticular endothelial system (RES). A liposome formulation that can facilitate the association of drug with the surface of cells, such as, lymphocytes and macrophages is also useful. This approach may provide enhanced delivery of the drug to target cells by taking advantage of the specificity of macrophage and lymphocyte immune recognition of abnormal cells, such as cancer cells.

By "pharmaceutically acceptable formulation" is meant, a composition or formulation that allows for the effective distribution of the nucleic acid molecules of the instant invention in the physical location most suitable for their desired activity. Nonlimiting examples of agents suitable for formulation with the nucleic acid molecules of the instant invention include: P-glycoprotein inhibitors (such as Pluronic P85), which can enhance entry of drugs into the CNS (Joliet-Riant and Tillement, 1999, *Fundam. Clin. Pharmacol.*, 13, 16-26); biodegradable polymers, such as poly (DL-lactide-coglycolide) microspheres for sustained release delivery after intracerebral implantation (Emerich, DF *et al.*, 1999, *Cell Transplant*, 8, 47-58) (Alkermes, Inc. Cambridge, MA); and loaded nanoparticles, such as those made of polybutylcyanoacrylate, which can deliver drugs across the blood brain barrier and can alter neuronal uptake mechanisms (*Prog Neuropsychopharmacol Biol Psychiatry*, 23, 941-949, 1999). Other non-limiting examples of delivery strategies for the nucleic acid molecules of the instant invention include material described in Boado *et al.*, 1998, *J. Pharm. Sci.*, 87, 1308-1315; Tyler *et al.*, 1999, *FEBS Lett.*, 421, 280-284; Pardridge *et al.*, 1995, *PNAS USA*, 92, 5592-5596; Boado, 1995, *Adv. Drug Delivery Rev.*, 15, 73-107; Aldrian-Herrada *et al.*, 1998, *Nucleic Acids Res.*, 26, 4910-4916; and Tyler *et al.*, 1999, *PNAS USA*, 96, 7053-7058.

The invention also features the use of the composition comprising surface-modified liposomes containing poly (ethylene glycol) lipids (PEG-modified, or long-circulating

liposomes or stealth liposomes). These formulations offer a method for increasing the accumulation of drugs in target tissues. This class of drug carriers resists opsonization and elimination by the mononuclear phagocytic system (MPS or RES), thereby enabling longer blood circulation times and enhanced tissue exposure for the encapsulated drug (Lasic *et al.* *Chem. Rev.* 1995, 95, 2601-2627; Ishiwata *et al.*, *Chem. Pharm. Bull.* 1995, 43, 1005-1011). Such liposomes have been shown to accumulate selectively in tumors, presumably by extravasation and capture in the neovascularized target tissues (Lasic *et al.*, *Science* 1995, 267, 1275-1276; Oku *et al.*, 1995, *Biochim. Biophys. Acta*, 1238, 86-90). The long-circulating liposomes enhance the pharmacokinetics and pharmacodynamics of DNA and RNA, particularly compared to conventional cationic liposomes which are known to accumulate in tissues of the MPS (Liu *et al.*, *J. Biol. Chem.* 1995, 270, 24864-24870; Choi *et al.*, International PCT Publication No. WO 96/10391; Ansell *et al.*, International PCT Publication No. WO 96/10390; Holland *et al.*, International PCT Publication No. WO 96/10392). Long-circulating liposomes are also likely to protect drugs from nuclease degradation to a greater extent compared to cationic liposomes, based on their ability to avoid accumulation in metabolically aggressive MPS tissues such as the liver and spleen.

The present invention also includes compositions prepared for storage or administration, which include a pharmaceutically effective amount of the desired compounds in a pharmaceutically acceptable carrier or diluent. Acceptable carriers or diluents for therapeutic use are well known in the pharmaceutical art, and are described, for example, in *Remington's Pharmaceutical Sciences*, Mack Publishing Co. (A.R. Gennaro edit. 1985) hereby incorporated by reference herein. For example, preservatives, stabilizers, dyes and flavoring agents may be provided. These include sodium benzoate, sorbic acid and esters of *p*-hydroxybenzoic acid. In addition, antioxidants and suspending agents may be used.

A pharmaceutically effective dose is that dose required to prevent, inhibit the occurrence of, or treat (alleviate a symptom to some extent, preferably all of the symptoms) a disease state. The pharmaceutically effective dose depends on the type of disease, the composition used, the route of administration, the type of mammal being treated, the physical characteristics of the specific mammal under consideration, concurrent medication, and other factors that those skilled in the medical arts will recognize. Generally, an amount between 0.1 mg/kg and 100 mg/kg body weight/day of active ingredients is administered dependent upon potency of the negatively charged polymer.

The present invention also includes compositions prepared for storage or administration that include a pharmaceutically effective amount of the desired compounds in a pharmaceutically acceptable carrier or diluent. Acceptable carriers or diluents for therapeutic use are well known in the pharmaceutical art, and are described, for example, in *Remington's*

Pharmaceutical Sciences, Mack Publishing Co. (A.R. Gennaro edit. 1985), hereby incorporated by reference herein. For example, preservatives, stabilizers, dyes and flavoring agents can be provided. These include sodium benzoate, sorbic acid and esters of *p*-hydroxybenzoic acid. In addition, antioxidants and suspending agents can be used.

A pharmaceutically effective dose is that dose required to prevent, inhibit the occurrence, or treat (alleviate a symptom to some extent, preferably all of the symptoms) of a disease state. The pharmaceutically effective dose depends on the type of disease, the composition used, the route of administration, the type of mammal being treated, the physical characteristics of the specific mammal under consideration, concurrent medication, and other factors that those skilled in the medical arts will recognize. Generally, an amount between 0.1 mg/kg and 100 mg/kg body weight/day of active ingredients is administered dependent upon potency of the negatively charged polymer.

The nucleic acid molecules of the invention and formulations thereof can be administered orally, topically, parenterally, by inhalation or spray, or rectally in dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and/or vehicles. The term parenteral as used herein includes percutaneous, subcutaneous, intravascular (*e.g.*, intravenous), intramuscular, or intrathecal injection or infusion techniques and the like. In addition, there is provided a pharmaceutical formulation comprising a nucleic acid molecule of the invention and a pharmaceutically acceptable carrier. One or more nucleic acid molecules of the invention can be present in association with one or more non-toxic pharmaceutically acceptable carriers and/or diluents and/or adjuvants, and if desired other active ingredients. The pharmaceutical compositions containing nucleic acid molecules of the invention can be in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsion, hard or soft capsules, or syrups or elixirs.

Compositions intended for oral use can be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions can contain one or more such sweetening agents, flavoring agents, coloring agents or preservative agents in order to provide pharmaceutically elegant and palatable preparations. Tablets contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients that are suitable for the manufacture of tablets. These excipients can be, for example, inert diluents; such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, for example, corn starch, or alginic acid; binding agents, for example starch, gelatin or acacia; and lubricating agents, for example magnesium stearate, stearic acid or talc. The tablets can be uncoated or they can be coated by known techniques. In some cases such coatings can be prepared by

known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate can be employed.

Formulations for oral use can also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium, for example peanut oil, liquid paraffin or olive oil.

Aqueous suspensions contain the active materials in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydropropyl-methylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents can be a naturally-occurring phosphatide, for example, lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethyleneoxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions can also contain one or more preservatives, for example ethyl, or n-propyl p-hydroxybenzoate, one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose or saccharin.

Oily suspensions can be formulated by suspending the active ingredients in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil, or in a mineral oil such as liquid paraffin. The oily suspensions can contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents and flavoring agents can be added to provide palatable oral preparations. These compositions can be preserved by the addition of an anti-oxidant such as ascorbic acid.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents or suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavoring and coloring agents, can also be present.

Pharmaceutical compositions of the invention can also be in the form of oil-in-water emulsions. The oily phase can be a vegetable oil or a mineral oil or mixtures of these. Suitable emulsifying agents can be naturally-occurring gums, for example gum acacia or gum

tragacanth, naturally-occurring phosphatides, for example soy bean, lecithin, and esters or partial esters derived from fatty acids and hexitol, anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions can also contain sweetening and flavoring agents.

Syrups and elixirs can be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol, glucose or sucrose. Such formulations can also contain a demulcent, a preservative and flavoring and coloring agents. The pharmaceutical compositions can be in the form of a sterile injectable aqueous or oleaginous suspension. This suspension can be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents that have been mentioned above. The sterile injectable preparation can also be a sterile injectable solution or suspension in a non-toxic parentally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that can be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose, any bland fixed oil can be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

The nucleic acid molecules of the invention can also be administered in the form of suppositories, *e.g.*, for rectal administration of the drug. These compositions can be prepared by mixing the drug with a suitable non-irritating excipient that is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials include cocoa butter and polyethylene glycols.

Nucleic acid molecules of the invention can be administered parenterally in a sterile medium. The drug, depending on the vehicle and concentration used, can either be suspended or dissolved in the vehicle. Advantageously, adjuvants such as local anesthetics, preservatives and buffering agents can be dissolved in the vehicle.

Dosage levels of the order of from about 0.1 mg to about 140 mg per kilogram of body weight per day are useful in the treatment of the above-indicated conditions (about 0.5 mg to about 7 g per patient per day). The amount of active ingredient that can be combined with the carrier materials to produce a single dosage form varies depending upon the host treated and the particular mode of administration. Dosage unit forms generally contain between from about 1 mg to about 500 mg of an active ingredient.

It is understood that the specific dose level for any particular patient depends upon a variety of factors including the activity of the specific compound employed, the age, body

weight, general health, sex, diet, time of administration, route of administration, and rate of excretion, drug combination and the severity of the particular disease undergoing therapy.

For administration to non-human animals, the composition can also be added to the animal feed or drinking water. It can be convenient to formulate the animal feed and drinking water compositions so that the animal takes in a therapeutically appropriate quantity of the composition along with its diet. It can also be convenient to present the composition as a premix for addition to the feed or drinking water.

The nucleic acid molecules of the present invention may also be administered to a patient in combination with other therapeutic compounds to increase the overall therapeutic effect. The use of multiple compounds to treat an indication may increase the beneficial effects while reducing the presence of side effects.

In one embodiment, the invention compositions suitable for administering nucleic acid molecules of the invention to specific cell types, such as hepatocytes. For example, the asialoglycoprotein receptor (ASGPr) (Wu and Wu, 1987, *J. Biol. Chem.* 262, 4429-4432) is unique to hepatocytes and binds branched galactose-terminal glycoproteins, such as asialoorosomucoid (ASOR). Binding of such glycoproteins or synthetic glycoconjugates to the receptor takes place with an affinity that strongly depends on the degree of branching of the oligosaccharide chain, for example, triantennary structures are bound with greater affinity than biantennary or monoantennary chains (Baenziger and Fiete, 1980, *Cell*, 22, 611-620; Connolly *et al.*, 1982, *J. Biol. Chem.*, 257, 939-945). Lee and Lee, 1987, *Glycoconjugate J.*, 4, 317-328, obtained this high specificity through the use of N-acetyl-D-galactosamine as the carbohydrate moiety, which has higher affinity for the receptor, compared to galactose. This "clustering effect" has also been described for the binding and uptake of mannosyl-terminating glycoproteins or glycoconjugates (Ponpipom *et al.*, 1981, *J. Med. Chem.*, 24, 1388-1395). The use of galactose and galactosamine based conjugates to transport exogenous compounds across cell membranes can provide a targeted delivery approach to the treatment of liver disease such as HBV infection or hepatocellular carcinoma. The use of bioconjugates can also provide a reduction in the required dose of therapeutic compounds required for treatment. Furthermore, therapeutic bioavailability, pharmacodynamics, and pharmacokinetic parameters can be modulated through the use of nucleic acid bioconjugates of the invention.

Alternatively, certain of the nucleic acid molecules of the instant invention can be expressed within cells from eukaryotic promoters (*e.g.*, Izant and Weintraub, 1985, *Science*, 229, 345; McGarry and Lindquist, 1986, *Proc. Natl. Acad. Sci. USA* 83, 399; Scanlon *et al.*, 1991, *Proc. Natl. Acad. Sci. USA*, 88, 10591-5; Kashani-Sabet *et al.*, 1992, *Antisense Res. Dev.*, 2, 3-15; Dropulic *et al.*, 1992, *J. Virol.*, 66, 1432-41; Weerasinghe *et al.*, 1991, *J. Virol.*, 65, 5531-4; Ojwang *et al.*, 1992, *Proc. Natl. Acad. Sci. USA*, 89, 10802-6; Chen *et*

al., 1992, *Nucleic Acids Res.*, 20, 4581-9; Sarver *et al.*, 1990 *Science*, 247, 1222-1225; Thompson *et al.*, 1995, *Nucleic Acids Res.*, 23, 2259; Good *et al.*, 1997, *Gene Therapy*, 4, 45; all of these references are hereby incorporated in their totalities by reference herein). Those skilled in the art realize that any nucleic acid can be expressed in eukaryotic cells from the appropriate DNA/RNA vector. The activity of such nucleic acids can be augmented by their release from the primary transcript by a ribozyme (Draper *et al.*, PCT WO 93/23569, and Sullivan *et al.*, PCT WO 94/02595; Ohkawa *et al.*, 1992, *Nucleic Acids Symp. Ser.*, 27, 15-6; Taira *et al.*, 1991, *Nucleic Acids Res.*, 19, 5125-30; Ventura *et al.*, 1993, *Nucleic Acids Res.*, 21, 3249-55; Chowrira *et al.*, 1994, *J. Biol. Chem.*, 269, 25856; all of these references are hereby incorporated in their totality by reference herein).

In another aspect of the invention, RNA molecules of the present invention are preferably expressed from transcription units (see, for example, Couture *et al.*, 1996, *TIG.*, 12, 510) inserted into DNA or RNA vectors. The recombinant vectors are preferably DNA plasmids or viral vectors. Ribozyme expressing viral vectors could be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, the recombinant vectors capable of expressing the nucleic acid molecules are delivered as described above, and persist in target cells. Alternatively, viral vectors may be used that provide for transient expression of nucleic acid molecules. Such vectors might be repeatedly administered as necessary. Once expressed, the nucleic acid molecule binds to the target mRNA. Delivery of nucleic acid molecule expressing vectors could be systemic, such as by intravenous or intra-muscular administration, by administration to target cells ex-planted from the patient followed by reintroduction into the patient, or by any other means that would allow for introduction into the desired target cell (for a review see Couture *et al.*, 1996, *TIG.*, 12, 510).

In one aspect, the invention features an expression vector comprising a nucleic acid sequence encoding at least one of the nucleic acid molecules of the instant invention is disclosed. The nucleic acid sequence encoding the nucleic acid molecule of the instant invention is operable linked in a manner which allows expression of that nucleic acid molecule.

In another aspect the invention features an expression vector comprising: a) a transcription initiation region (*e.g.*, eukaryotic pol I, II or III initiation region); b) a transcription termination region (*e.g.*, eukaryotic pol I, II or III termination region); c) a nucleic acid sequence encoding at least one of the nucleic acid catalyst of the instant invention; and wherein said sequence is operably linked to said initiation region and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule. The vector may optionally include an open reading frame (ORF) for a protein

operably linked on the 5' side or the 3'-side of the sequence encoding the nucleic acid catalyst of the invention; and/or an intron (intervening sequences).

Transcription of the nucleic acid molecule sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, etc.) present nearby. Prokaryotic RNA polymerase promoters are also used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells (Elroy-Stein and Moss, 1990, *Proc. Natl. Acad. Sci. U S A*, 87, 6743-7; Gao and Huang 1993, *Nucleic Acids Res.*, 21, 2867-72; Lieber et al., 1993, *Methods Enzymol.*, 217, 47-66; Zhou et al., 1990, *Mol. Cell. Biol.*, 10, 4529-37). All of these references are incorporated by reference herein. Several investigators have demonstrated that nucleic acid molecules, such as ribozymes expressed from such promoters can function in mammalian cells (e.g. Kashani-Sabet et al., 1992, *Antisense Res. Dev.*, 2, 3-15; Ojwang et al., 1992, *Proc. Natl. Acad. Sci. U S A*, 89, 10802-6; Chen et al., 1992, *Nucleic Acids Res.*, 20, 4581-9; Yu et al., 1993, *Proc. Natl. Acad. Sci. U S A*, 90, 6340-4; L'Huillier et al., 1992, *EMBO J.*, 11, 4411-8; Lisiewicz et al., 1993, *Proc. Natl. Acad. Sci. U. S. A*, 90, 8000-4; Thompson et al., 1995, *Nucleic Acids Res.*, 23, 2259; Sullenger & Cech, 1993, *Science*, 262, 1566). More specifically, transcription units such as the ones derived from genes encoding U6 small nuclear (snRNA), transfer RNA (tRNA) and adenovirus VA RNA are useful in generating high concentrations of desired RNA molecules such as ribozymes in cells (Thompson et al., *supra*; Couture and Stinchcomb, 1996, *supra*; Noonberg et al., 1994, *Nucleic Acid Res.*, 22, 2830; Noonberg et al., US Patent No. 5,624,803; Good et al., 1997, *Gene Ther.*, 4, 45; Beigelman et al., International PCT Publication No. WO 96/18736; all of these publications are incorporated by reference herein). The above ribozyme transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated virus vectors), or viral RNA vectors (such as retroviral or alphavirus vectors) (for a review see Couture and Stinchcomb, 1996, *supra*).

In yet another aspect, the invention features an expression vector comprising nucleic acid sequence encoding at least one of the nucleic acid molecules of the invention, in a manner that allows expression of that nucleic acid molecule. The expression vector comprises in one embodiment; a) a transcription initiation region; b) a transcription termination region; c) a nucleic acid sequence encoding at least one said nucleic acid molecule; and wherein said sequence is operably linked to said initiation region and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule. In another embodiment, the expression vector comprises: a) a transcription initiation region; b) a

transcription termination region; c) an open reading frame; d) a nucleic acid sequence encoding at least one said nucleic acid molecule, wherein said sequence is operably linked to the 3'-end of said open reading frame; and wherein said sequence is operably linked to said initiation region, said open reading frame and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule. In yet another embodiment, the expression vector comprises: a) a transcription initiation region; b) a transcription termination region; c) an intron; d) a nucleic acid sequence encoding at least one said nucleic acid molecule; and wherein said sequence is operably linked to said initiation region, said intron and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule. In another embodiment, the expression vector comprises: a) a transcription initiation region; b) a transcription termination region; c) an intron; d) an open reading frame; e) a nucleic acid sequence encoding at least one said nucleic acid molecule, wherein said sequence is operably linked to the 3'-end of said open reading frame; and wherein said sequence is operably linked to said initiation region, said intron, said open reading frame and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule.

Interferons

Type I interferons (IFN) are a class of natural cytokines that includes a family of greater than 25 IFN- α (Pesta, 1986, *Methods Enzymol.* 119, 3-14) as well as IFN- β , and IFN- ω . Although evolutionarily derived from the same gene (Diaz *et al.*, 1994, *Genomics* 22, 540-552), there are many differences in the primary sequence of these molecules, implying an evolutionary divergence in biologic activity. All type I IFN share a common pattern of biologic effects that begin with binding of the IFN to the cell surface receptor (Pfeffer & Strulovici, 1992, Transmembrane secondary messengers for IFN- α/β . In: *Interferon. Principles and Medical Applications.*, S. Baron, D.H. Coopenhaver, F. Dianzani, W.R. Fleischmann Jr., T.K. Hughes Jr., G.R. Kimpel, D.W. Niesel, G.J. Stanton, and S.K. Tying, eds. 151-160). Binding is followed by activation of tyrosine kinases, including the Janus tyrosine kinases and the STAT proteins, which leads to the production of several IFN-stimulated gene products (Johnson *et al.*, 1994, *Sci. Am.* 270, 68-75). The IFN-stimulated gene products are responsible for the pleiotropic biologic effects of type I IFN, including antiviral, antiproliferative, and immunomodulatory effects, cytokine induction, and HLA class I and class II regulation (Pestka *et al.*, 1987, *Annu. Rev. Biochem* 56, 727). Examples of IFN-stimulated gene products include 2-5-oligoadenylate synthetase (2-5 OAS), β_2 -microglobulin, neopterin, p68 kinases, and the Mx protein (Chebath & Revel, 1992, The 2-5 A system: 2-5 A synthetase, isospecies and functions. In: *Interferon. Principles and Medical Applications.* S. Baron, D.H. Coopenhaver, F. Dianzani, W.R. Jr. Fleischmann, T.K. Jr Hughes, G.R. Kimpel, D.W. Niesel, G.J. Stanton, and S.K. Tying, eds., pp. 225-236;

Samuel, 1992, The RNA-dependent P1/eIF-2 α protein kinase. In: *Interferon. Principles and Medical Applications*. S. Baron, D.H. Coopenhaver, F. Dianzani, W.R. Fleischmann Jr., T.K. Hughes Jr., G.R. Kimpel, D.W. Niesel, G.H. Stanton, and S.K. Tying, eds. 237-250; Horisberger, 1992, MX protein: function and Mechanism of Action. In: *Interferon. Principles and Medical Applications*. S. Baron, D.H. Coopenhaver, F. Dianzani, W.R. Fleischmann Jr., T.K. Hughes Jr., G.R. Kimpel, D.W. Niesel, G.H. Stanton, and S.K. Tying, eds. 215-224). Although all type I IFN have similar biologic effects, not all the activities are shared by each type I IFN, and, in many cases, the extent of activity varies quite substantially for each IFN subtype (Fish *et al.*, 1989, *J. Interferon Res.* 9, 97-114; Ozes *et al.*, 1992, *J. Interferon Res.* 12, 55-59). More specifically, investigations into the properties of different subtypes of IFN- α and molecular hybrids of IFN- α have shown differences in pharmacologic properties (Rubinstein, 1987, *J. Interferon Res.* 7, 545-551). These pharmacologic differences can arise from as few as three amino acid residue changes (Lee *et al.*, 1982, *Cancer Res.* 42, 1312-1316).

Eighty-five to 166 amino acids are conserved in the known IFN- α subtypes. Excluding the IFN- α pseudogenes, there are approximately 25 known distinct IFN- α subtypes. Pairwise comparisons of these nonallelic subtypes show primary sequence differences ranging from 2% to 23%. In addition to the naturally occurring IFNs, a non-natural recombinant type I interferon known as consensus interferon (CIFN) has been synthesized as a therapeutic compound (Tong *et al.*, 1997, *Hepatology* 26, 747-754).

Interferon is currently in use for at least 12 different indications including infectious and autoimmune diseases and cancer (Borden, 1992, *N. Engl. J. Med.* 326, 1491-1492). For autoimmune diseases IFN has been utilized for treatment of rheumatoid arthritis, multiple sclerosis, and Crohn's disease. For treatment of cancer IFN has been used alone or in combination with a number of different compounds. Specific types of cancers for which IFN has been used include squamous cell carcinomas, melanomas, hypernephromas, hemangiomas, hairy cell leukemia, and Kaposi's sarcoma. In the treatment of infectious diseases, IFNs increase the phagocytic activity of macrophages and cytotoxicity of lymphocytes and inhibits the propagation of cellular pathogens. Specific indications for which IFN has been used as treatment include: hepatitis B, human papillomavirus types 6 and 11 (i.e. genital warts) (Leventhal *et al.*, 1991, *N Engl J Med* 325, 613-617), chronic granulomatous disease, and hepatitis C virus.

Numerous well controlled clinical trials using IFN-alpha in the treatment of chronic HCV infection have demonstrated that treatment three times a week results in lowering of serum ALT values in approximately 50% (range 40% to 70%) of patients by the end of 6 months of therapy (Davis *et al.*, 1989, *The new England Journal of Medicine* 321, 1501-

1506; Marcellin et al., 1991, *Hepatology* 13, 393-397; Tong *et al.*, 1997, *Hepatology* 26, 747-754; Tong et al., *Hepatology* 26, 1640-1645). However, following cessation of interferon treatment, approximately 50% of the responding patients relapsed, resulting in a "durable" response rate as assessed by normalization of serum ALT concentrations of approximately 20 to 25%. In addition, studies that have examined six months of type 1 interferon therapy using changes in HCV RNA values as a clinical endpoint have demonstrated that up to 35% of patients will have a loss of HCV RNA by the end of therapy (Tong *et al.*, 1997, *supra*). However, as with the ALT endpoint, about 50% of the patients relapse six months following cessation of therapy resulting in a durable virologic response of only 12% (23). Studies that have examined 48 weeks of therapy have demonstrated that the sustained virological response is up to 25%.

Pegylated interferons, ie. interferons conjugated with polyethylene glycol (PEG), have demonstrated improved characteristics over interferon. Advantages incurred by PEG conjugation can include an improved pharmacokinetic profile compared to interferons lacking PEG, thus imparting more convenient dosing regimes, improved tolerance, and improved antiviral efficacy. Such improvements have been demonstrated in clinical studies of both polyethylene glycol interferon alfa-2a (PEGASYS, Roche) and polyethylene glycol interferon alfa-2b (VIRAIFERON PEG, PEG-INTRON, Enzon/Schering Plough).

Enzymatic nucleic acid molecules in combination with interferons and polyethylene glycol interferons have the potential to improve the effectiveness of treatment of HCV or any of the other indications discussed above. Enzymatic nucleic acid molecules targeting RNAs associated with diseases such as infectious diseases, autoimmune diseases, and cancer, can be used individually or in combination with other therapies such as interferons and polyethylene glycol interferons and to achieve enhanced efficacy.

Examples:

The following are non-limiting examples showing the selection, isolation, synthesis and activity of nucleic acids of the instant invention. These examples demonstrate the selection and design of Antisense, Hammerhead, DNAzyme, NCH, Amberzyme, Zinzyme or G-Cleaver ribozyme molecules and binding/cleavage sites within HBV and HCV RNA. The following examples also demonstrate the selection and design of nucleic acid decoy molecules that target HBV reverse transcriptase. The following examples also demonstrate the use of enzymatic nucleic acid molecules that cleave HCV RNA. The methods described herein represent a scheme by which nucleic acid molecules can be derived that cleave other RNA targets required for HCV replication.

Example 1: Identification of Potential Target Sites in Human HBV RNA

The sequence of human HBV was screened for accessible sites using a computer-folding algorithm. Regions of the RNA that did not form secondary folding structures and contained potential ribozyme and/or antisense binding/cleavage sites were identified. The sequences of these cleavage sites are shown in **Tables IV - XI**.

Example 2: Selection of Enzymatic Nucleic Acid Cleavage Sites in Human HBV RNA

Ribozyme target sites were chosen by analyzing sequences of Human HBV (accession number: AF100308.1) and prioritizing the sites on the basis of folding. Ribozymes were designed that could bind each target and were individually analyzed by computer folding (Christoffersen *et al.*, 1994 *J. Mol. Struct. Theochem*, 311, 273; Jaeger *et al.*, 1989, *Proc. Natl. Acad. Sci. USA*, 86, 7706) to assess whether the ribozyme sequences fold into the appropriate secondary structure. Those ribozymes with unfavorable intramolecular interactions between the binding arms and the catalytic core were eliminated from consideration. As noted herein, varying binding arm lengths can be chosen to optimize activity. Generally, at least 5 bases on each arm are able to bind to, or otherwise interact with, the target RNA.

Example 3: Chemical Synthesis and Purification of Ribozymes and Antisense for Efficient Cleavage and/or blocking of HBV RNA

Ribozymes and antisense constructs were designed to anneal to various sites in the RNA message. The binding arms of the ribozymes are complementary to the target site sequences described above, while the antisense constructs are fully complementary to the target site sequences described above. The ribozymes and antisense constructs were chemically synthesized. The method of synthesis used followed the procedure for normal RNA synthesis as described above and in Usman *et al.*, (1987 *J. Am. Chem. Soc.*, 109, 7845), Scaringe *et al.*, (1990 *Nucleic Acids Res.*, 18, 5433) and Wincott *et al.*, *supra*, and made use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. The average stepwise coupling yields were typically >98%.

Ribozymes and antisense constructs were also synthesized from DNA templates using bacteriophage T7 RNA polymerase (Milligan and Uhlenbeck, 1989, *Methods Enzymol.* 180, 51). Ribozymes and antisense constructs were purified by gel electrophoresis using general methods or were purified by high pressure liquid chromatography (HPLC; see Wincott *et al.*, *supra*; the totality of which is hereby incorporated herein by reference) and were resuspended in water. The sequences of the chemically synthesized ribozymes used in this study are shown below in **Table XI**.

Example 4: Ribozyme Cleavage of HBV RNA Target *in vitro*

Ribozymes targeted to the human HBV RNA are designed and synthesized as described above. These ribozymes can be tested for cleavage activity *in vitro*, for example using the following procedure. The target sequences and the nucleotide location within the HBV RNA are given in Tables IV-XI.

Cleavage Reactions: Full-length or partially full-length, internally-labeled target RNA for ribozyme cleavage assay is prepared by *in vitro* transcription in the presence of [α - 32 P] CTP, passed over a G 50 Sephadex® column by spin chromatography and used as substrate RNA without further purification. Alternately, substrates are 5'- 32 P-end labeled using T4 polynucleotide kinase enzyme. Assays are performed by pre-warming a 2X concentration of purified ribozyme in ribozyme cleavage buffer (50 mM Tris-HCl, pH 7.5 at 37°C, 10 mM MgCl₂) and the cleavage reaction was initiated by adding the 2X ribozyme mix to an equal volume of substrate RNA (maximum of 1-5 nM) that was also pre-warmed in cleavage buffer. As an initial screen, assays are carried out for 1 hour at 37°C using a final concentration of either 40 nM or 1 mM ribozyme, *i.e.*, ribozyme excess. The reaction is quenched by the addition of an equal volume of 95% formamide, 20 mM EDTA, 0.05% bromophenol blue and 0.05% xylene cyanol after which the sample is heated to 95°C for 2 minutes, quick chilled and loaded onto a denaturing polyacrylamide gel. Substrate RNA and the specific RNA cleavage products generated by ribozyme cleavage are visualized on an autoradiograph of the gel. The percentage of cleavage is determined by Phosphor Imager® quantitation of bands representing the intact substrate and the cleavage products.

Example 5: Transfection of HepG2 Cells with psHBV-1 and Ribozymes

The human hepatocellular carcinoma cell line Hep G2 was grown in Dulbecco's modified Eagle media supplemented with 10% fetal calf serum, 2 mM glutamine, 0.1 mM nonessential amino acids, 1 mM sodium pyruvate, 25 mM Hepes, 100 units penicillin, and 100 µg/ml streptomycin. To generate a replication competent cDNA, prior to transfection the HBV genomic sequences are excised from the bacterial plasmid sequence contained in the psHBV-1 vector (Those skilled in the art understand that other methods may be used to generate a replication competent cDNA). This was done with an EcoRI and Hind III restriction digest. Following completion of the digest, a ligation was performed under dilute conditions (20 µg/ml) to favor intermolecular ligation. The total ligation mixture was then concentrated using Qiagen spin columns.

Secreted alkaline phosphatase (SEAP) was used to normalize the HBsAg levels to control for transfection variability. The pSEAP2-TK control vector was constructed by ligating a Bgl II-Hind III fragment of the pRL-TK vector (Promega), containing the herpes

simplex virus thymidine kinase promoter region, into *Bgl* II/*Hind* III digested pSEAP2-Basic (Clontech). Hep G2 cells were plated (3×10^4 cells/well) in 96-well microtiter plates and incubated overnight. A lipid/DNA/ribozyme complex was formed containing (at final concentrations) cationic lipid (15 $\mu\text{g/ml}$), prepared psHBV-1 (4.5 $\mu\text{g/ml}$), pSEAP2-TK (0.5 $\mu\text{g/ml}$), and ribozyme (100 μM). Following a 15 min. incubation at 37° C, the complexes were added to the plated Hep G2 cells. Media was removed from the cells 96 hr. post-transfection for HBsAg and SEAP analysis.

Transfection of the human hepatocellular carcinoma cell line, Hep G2, with replication competent HBV DNA results in the expression of HBV proteins and the production of virions. To investigate the potential use of ribozymes for the treatment of chronic HBV infection, a series of ribozymes that target the 3' terminus of the HBV genome have been synthesized. Ribozymes targeting this region have the potential to cleave all four major HBV RNA transcripts as well as the potential to block the production of HBV DNA by cleavage of the pregenomic RNA. To test the efficacy of these HBV ribozymes, they were co-transfected with HBV genomic DNA into Hep G2 cells, and the subsequent levels of secreted HBV surface antigen (HBsAg) were analyzed by ELISA. To control for variability in transfection efficiency, a control vector which expresses secreted alkaline phosphatase (SEAP), was also co-transfected. The efficacy of the HBV ribozymes was determined by comparing the ratio of HBsAg:SEAP and/or HBeAg:SEAP to that of a scrambled attenuated control (SAC) ribozyme. Twenty-five ribozymes (RPI18341, RPI18356, RPI18363, RPI18364, RPI18365, RPI18366, RPI18367, RPI18368, RPI18369, RPI18370, RPI18371, RPI18372, RPI18373, RPI18374, RPI18303, RPI18405, RPI18406, RPI18407, RPI18408, RPI18409, RPI18410, RPI18411, RPI18418, RPI18419, and RPI18422) have been identified which cause a reduction in the levels of HBsAg and/or HBeAg as compared to the corresponding SAC ribozyme. In addition, loop variant anti-HBV ribozymes targeting site 273 were tested using this system, the results of this study are summarized in **Figure 10**. As indicated in the figure, the ribozymes tested demonstrate significant reduction in HepG2 HBsAg levels as compared to a scrambled attenuated core ribozyme control, with RPI 22650 and RPI 22649 showing the greatest decrease in HBsAg levels.

Example 6: Analysis of HBsAg and SEAP Levels Following Ribozyme Treatment

Immulon 4 (Dynax) microtiter wells were coated overnight at 4° C with anti-HBsAg Mab (Biostride B88-95-31ad,ay) at 1 $\mu\text{g/ml}$ in Carbonate Buffer (Na_2CO_3 15 mM, NaHCO_3 35 mM, pH 9.5). The wells were then washed 4x with PBST (PBS, 0.05% Tween® 20) and blocked for 1 hr at 37° C with PBST, 1% BSA. Following washing as above, the wells were dried at 37° C for 30 min. Biotinylated goat anti-HBsAg (Accurate YVS1807) was diluted 1:1000 in PBST and incubated in the wells for 1 hr. at 37° C. The wells were washed 4x with

PBST. Streptavidin/Alkaline Phosphatase Conjugate (Pierce 21324) was diluted to 250 ng/ml in PBST, and incubated in the wells for 1 hr. at 37° C. After washing as above, p-nitrophenyl phosphate substrate (Pierce 37620) was added to the wells, which were then incubated for 1 hr. at 37° C. The optical density at 405 nm was then determined. SEAP levels were assayed using the Great EscAPe® Detection Kit (Clontech K2041-1), as per the manufacturers instructions.

Example 7: X-gene Reporter Assay

The effect of ribozyme treatment on the level of transactivation of a SV40 promoter driven firefly luciferase gene by the HBV X-protein was analyzed in transfected Hep G2 cells. As a control for variability in transfection efficiency, a Renilla luciferase reporter driven by the TK promoter, which is not transactivated by the X protein, was used. Hep G2 cells were plated (3×10^4 cells/well) in 96-well microtiter plates and incubated overnight. A lipid/DNA/ribozyme complex was formed containing (at final concentrations) cationic lipid (2.4 µg/ml), the X-gene vector pSBDR(2.5 µg/ml), the firefly reporter pSV40HCVluc (0.5 µg/ml), the Renilla luciferase control vector pRL-TK (0.5 µg/ml), and ribozyme (100 µM). Following a 15 min. incubation at 37° C, the complexes were added to the plated Hep G2 cells. Levels of firefly and Renilla luciferase were analyzed 48 hr. post transfection, using Promega's Dual-Luciferase Assay System.

The HBV X protein is a transactivator of a number of viral and cellular genes. Ribozymes which target the X region were tested for their ability to cause a reduction in X protein transactivation of a firefly luciferase gene driven by the SV40 promoter in transfected Hep G2 cells. As a control for transfection variability, a vector containing the Renilla luciferase gene driven by the TK promoter, which is not activated by the X protein, was included in the co-transfections. The efficacy of the HBV ribozymes was determined by comparing the ratio of firefly luciferase: Renilla luciferase to that of a scrambled attenuated control (SAC) ribozyme. Eleven ribozymes (RPI18365, RPI18367, RPI18368, RPI18371, RPI18372, RPI18373, RPI18405, RPI18406, RPI18411, RPI18418, RPI18423) were identified which cause a reduction in the level of transactivation of a reporter gene by the X protein, as compared to the corresponding SAC ribozyme.

Example 8: HBV transgenic mouse study A

A transgenic mouse strain (founder strain 1.3.32 with a C57B1/6 background) that expresses HBV RNA and forms HBV viremia (Morrey *et al.*, 1999, *Antiviral Res.*, 42, 97-108; Guidotti *et al.*, 1995, *J. Virology*, 69, 10, 6158-6169) was utilized to study the *in vivo* activity of ribozymes (RPI.18341, RPI.18371, RPI.18372, and RPI.18418) of the instant invention. This model is predictive in screening for anti-HBV agents. Ribozyme or the

equivalent volume of saline was administered via a continuous s.c. infusion using Alzet® mini-osmotic pumps for 14 days. Alzet® pumps were filled with test material(s) in a sterile fashion according to the manufacturer's instructions. Prior to *in vivo* implantation, pumps were incubated at 37°C overnight (≥ 18 hours) to prime the flow modulators. On the day of surgery, animals were lightly anesthetized with a ketamine/xylazine cocktail (94 mg/kg and 6 mg/kg, respectively; 0.3 ml, IP). Baseline blood samples (200 μ l) were obtained from each animal *via* a retro-orbital bleed. For animals in groups 1-5 (Table XII), a 2 cm area near the base of the tail was shaved and cleansed with betadine surgical scrub and sequentially with 70% alcohol. A 1 cm incision in the skin was made with a #15 scalpel blade or a blunt pair of scissors near the base of the tail. Forceps were used to open a pocket rostrally (*ie.*, towards the head) by spreading apart the subcutaneous connective tissue. The pump was inserted with the delivery portal pointing away from the incision. Wounds were closed with sterile 9-mm stainless steel clips or with sterile 4-0 suture. Animals were then allowed to recover from anesthesia on a warm heating pad before being returned to their cage. Wounds were checked daily. Clips or sutures were replaced as needed. Incisions typically healed completely within 7 days post-op. Animals were then deeply anesthetized with the ketamine/xylazine cocktail (150 mg/kg and 10 mg/kg, respectively; 0.5 ml, IP) on day 14 post pump implantation. A midline thoracotomy/ laparotomy was performed to expose the abdominal cavity and the thoracic cavity. The left ventricle was cannulated at the base and animals exsanguinated using a 23G needle and 1 ml syringe. Serum was separated, frozen and analyzed for HBV DNA and antigen levels. Experimental groups were compared to the saline control group in respect to percent change from day 0 to day 14. HBV DNA was assayed by quantitative PCR.

Results

Table XII is a summary of the group designation and dosage levels used in this HBV transgenic mouse study. Baseline blood samples were obtained *via* a retroorbital bleed and animals (N=10/group) received anti-HBV ribozymes (100 mg/kg/day) as a continuous SC infusion. After 14 days, animals treated with a ribozyme targeting site 273 (RPI.18341) of the HBV RNA showed a significant reduction in serum HBV DNA concentration, compared to the saline treated animals as measured by a quantitative PCR assay. More specifically, the saline treated animals had a 69% increase in serum HBV DNA concentrations over this 2-week period while treatment with the 273 ribozyme (RPI.18341) resulted in a 60% decrease in serum HBV DNA concentrations. Ribozymes directed against sites 1833 (RPI.18371), 1873 (RPI.18418), and 1874 (RPI.18372) decreased serum HBV DNA concentrations by 49%, 15% and 16%, respectively.

Example 9: HBV transgenic mouse study B

A transgenic mouse strain (founder strain 1.3.32 with a C57B1/6 background) that expresses HBV RNA and forms HBV viremia (Morrey *et al.*, 1999, *Antiviral Res.*, 42, 97-108; Guidotti *et al.*, 1995, *J. Virology*, 69, 10, 6158-6169) was utilized to study the *in vivo* activity of ribozymes (RPI.18341 and RPI.18371) of the instant invention. This model is predictive in screening for anti-HBV agents. Ribozyme or the equivalent volume of saline was administered via a continuous s.c. infusion using Alzet® mini-osmotic pumps for 14 days. Alzet® pumps were filled with test material(s) in a sterile fashion according to the manufacturer's instructions. Prior to *in vivo* implantation, pumps were incubated at 37°C overnight (≥ 18 hours) to prime the flow modulators. On the day of surgery, animals were lightly anesthetized with a ketamine/xylazine cocktail (94 mg/kg and 6 mg/kg, respectively; 0.3 ml, IP). Baseline blood samples (200 μ l) were obtained from each animal *via* a retro-orbital bleed. For animals in groups 1-10 (Table XIII), a 2 cm area near the base of the tail was shaved and cleansed with betadine surgical scrub and sequentially with 70% alcohol. A 1 cm incision in the skin was made with a #15 scalpel blade or a blunt pair of scissors near the base of the tail. Forceps were used to open a pocket rostrally (*ie.*, towards the head) by spreading apart the subcutaneous connective tissue. The pump was inserted with the delivery portal pointing away from the incision. Wounds were closed with sterile 9-mm stainless steel clips or with sterile 4-0 suture. Animals were then allowed to recover from anesthesia on a warm heating pad before being returned to their cage. Wounds were checked daily. Clips or sutures were replaced as needed. Incisions typically healed completely within 7 days post-op. Animals were then deeply anesthetized with the ketamine/xylazine cocktail (150 mg/kg and 10 mg/kg, respectively; 0.5 ml, IP) on day 14 post pump implantation. A midline thoracotomy/ laparotomy was performed to expose the abdominal cavity and the thoracic cavity. The left ventricle was cannulated at the base and animals exsanguinated using a 23G needle and 1 ml syringe. Serum was separated, frozen and analyzed for HBV DNA and antigen levels. Experimental groups were compared to the saline control group in respect to percent change from day 0 to day 14. HBV DNA was assayed by quantitative PCR. Additionally, mice treated with 3TC® by oral gavage at a dose of 300 mg/kg/day for 14 days (group 11, Table XIII) were used as a positive control.

Results

Table XIII is a summary of the group designation and dosage levels used in this HBV transgenic mouse study. Baseline blood samples were obtained *via* a retroorbital bleed and animals (N=15/group) received anti-HBV ribozymes (100 mg/kg/day, 30 mg/kg/day, 10 mg/kg/day) as a continuous SC infusion. The results of this study are summarized in **Figures 6, 7, and 8**. As **Figures 6, 7, and 8** demonstrate, Ribozymes directed against sites 273 (RPI.18341) and 1833 (RPI.18371) demonstrate reduction in the serum HBV DNA levels following 14 days of ribozyme treatment in HBV transgenic mice, as compared to scrambled attenuated core (SAC) ribozyme and saline controls. Furthermore, these ribozymes provide similar, and in some cases, greater reduction of serum HBV DNA levels, as compared to the 3TC® positive control, at lower doses than the 3TC® positive control.

Example 10: HBV DNA reduction in HepG2.2.15 cells

Ribozyme treatment of HepG2.2.15 cells was performed in a 96-well plate format, with 12 wells for each different ribozyme tested (RPI.18341, RPI.18371, RPI.18372, RPI.18418, RPI.20599SAC). HBV DNA levels in the media collected between 120 and 144 hours following transfection was determined using the Roche Amplicor HBV Assay. Treatment with RPI.18341 targeting site 273 resulted in a significant ($P<0.05$) decrease in HBV DNA levels of 62% compared to the SAC (RPI.20599). Treatment with RPI.18371 (site 1833) or RPI.18372 (site 1874) resulted in reductions in HBV DNA levels of 55% and 58% respectively, as compared to treatment with the SAC RPI.20599 (see **Figure 9**).

Example 11: RPI 18341 combination treatment with Lamivudine/Infergen®

The therapeutic use of nucleic acid molecules of the invention either alone or in combination with current therapies, for example lamivudine or type 1 IFN, can lead to improved HBV treatment modalities. To assess the potential of combination therapy, HepG2 cells transfected with a replication competent HBV cDNA, were treated with RPI 18341 (HepBzyme™), Infergen® (Amgen, Thousand Oaks Ca), and/or Lamivudine (Epivir®: GlaxoSmithKline, Research Triangle Park NC) either alone or in combination. Results indicated that combination treatment with either RPI 18341 plus Infergen® or combination of RPI 18341 plus lamivudine results in additive down regulation of HBsAg expression ($P<0.001$). These studies can be applied to the treatment of lamivudine resistant cells to further assess the potential for combination therapy of RPI 18341 plus currently available therapies for the treatment of chronic Hepatitis B.

Hep G2 cells were plated (2×10^4 cells/well) in 96-well microtiter plates and incubated overnight. A cationic lipid/DNA/ribozyme complex was formed containing (at final

concentrations) lipid (11-15 $\mu\text{g/mL}$), re-ligated psHBV-1 (4.5 $\mu\text{g/mL}$) and ribozyme (100-200 nM) in growth media. Following a 15 min incubation at 37°C, 20 μL of the complex was added to the plated Hep G2 cells in 80 μL of growth media minus antibiotics. For combination treatment with interferon, interferon (Infergen®, Amgen, Thousand Oaks CA) was added at 24 hr post-transfection and then incubated for an additional 96 hr. In the case of co-treatment with Lamivudine (3TC®), the ribozyme-containing cell culture media was removed at 120 hr post-transfection, fresh media containing Lamivudine (Epivir®: GlaxoSmithKline, Research Triangle Park NC) was added, and then incubated for an additional 48 hours. Treatment with Lamivudine or interferon individually was done on Hep G2 cells transfected with the pSHBV-1 vector alone and then treated identically to the co-treated cells. All transfections were performed in triplicate. Analysis of HBsAg levels was performed using the Diasorin HBsAg ELISA kit.

Results

At either 500 or 1000 units of Infergen®, the addition of 200 nM of RPI.18341 results in a 75-77% increase in anti-HBV activity as judged by the level of HBsAg secreted from the treated Hep G2 cells. Conversely, the anti-HBV activity of RPI.18341(at 200 nM) is increased 31-39% when used in combination of 500 or 1000 units of Infergen® (Figure 11).

At 25 nM Lamivudine (3TC®), the addition of 100 nM of RPI.18341 results in a 48% increase in anti-HBV activity as judged by the level of HBsAg secreted from treated Hep G2 cells. Conversely, the anti-HBV activity of RPI.18341 (at 100 nM) is increased 31% when used in combination with 25 nM Lamivudine (Figure 12).

Example 13: Modulation of HBV reverse transcriptase

The HBV reverse transcriptase (pol) binds to the 5' stem-loop structure in the HBV pregenomic RNA and synthesizes a four-nucleotide primer from the template UUCA. The reverse transcriptase then translocates to the 3' end of the pregenomic RNA where the primer binds to the UUCA sequence within the DR1 element and begins first-strand synthesis of HBV DNA. A number of short oligos, ranging in size from 4 to 16-mers, were designed to act as competitive inhibitors of the HBV reverse transcriptase primer, either by blocking the primer binding sites on the HBV RNA or by acting as a decoy.

The oligonucleotides and controls were synthesized in all 2'-O-methyl and 2'-O-allyl versions (Table XV). The inverse sequence of all oligos were generated to serve as controls. Primary screening of the competitive inhibitors was completed in the HBsAg transfection/ELISA system, in which the oligo is co-transfected with a HBV cDNA vector into Hep G2 cells. Following 4 days of incubation, the levels of HBsAg secreted into the cell

culture media were determined by ELISA. Screening of the 2'-O-allyl versions revealed that two of the decoy oligos (RPI.24944 and RPI.24945), consisting of 3x or 4x repeats of the RT primer binding site UUCA, along with the matched inverse controls, displayed considerable activity by decreasing HBsAg levels (**Figure 15**). This dramatic decrease in HBsAg levels is not due to cellular toxicity, because a MTS assay showed no difference in proliferation between any of the treated cells. A follow up experiment with a 5x UUCA repeat, the inverse sequence control, and a matched scrambled control, showed that all three oligos decreased HBsAg levels without cellular toxicity. Screening of the 2'-O-methyl versions of the oligos showed no activity from the 3x and 4x UUCA repeat (**Figure 16**), also suggesting that the anti-HBV effect is perhaps related to the 2'-O-allyl chemistry rather than to sequence specificity.

Screening of the 2'-O-methyl oligos did show that the 2'-O-methyl 2x UUCA repeat, RPI.24986, displayed activity in decreasing HBsAg levels as compared to the inverse control, RPI.24950. A dose response experiment showed that at the lower concentrations of 100 and 200 nM, RPI.24986 showed greater activity in decreasing HbsAg levels as compared to the inverse control RPI.24950 (**Figure 17**).

Example 14: Modulation of HBV transcription via Oligonucleotides targeting the Enhancer I core region of HBV DNA

In an effort to block HBV replication, oligonucleotides were designed to bind to two liver-specific factor binding sites in the Enhancer I core region of HBV genomic DNA. Hepatocyte Nuclear Factor 3 (HNF3) and Hepatocyte Nuclear Factor 4 (HNF4) bind to sites in the core region, with the HNF3 site being 5' to the HNF4 site. The HNF3 and HNF4 sites overlap or are adjacent to binding sites for a number of more ubiquitous factors, and are termed nuclear receptor response elements (NRRE). These elements are critical in regulating HBV transcription and replication in infected hepatocytes, with mutations in the HNF3 and HNF4 binding sites having been demonstrated to greatly reduce the levels of HBV replication (Bock *et al.*, 2000, *J. Virology*, 74, 2193)

Oligonucleotides (**Table XV**) were designed to bind to either the positive or negative strands of the HNF3 or HNF4 binding sites. Scrambled controls were made to match each oligo. Each oligo was synthesized in all 2'-O-methyl/all phosphorothioate, or all 2'-O-allyl/all phosphorothioate chemistries. The initial screening of the oligos was done in the HBsAg transfection/ELISA system in Hep G2 cells. RPI.25654, which targets the negative strand of the HNF4 binding site, shows greater activity in reducing HBsAg levels as compared to RPI.25655, which targets the HNF4 site positive strand, and the scrambled control RPI.25656. This result was observed at both 200 and 400 nM (**Figures 18 and 19**).

In a follow-up study, RPL25654 reduced HBsAg levels in a dose-dependent manner, from 50-200 nM (Figure 20).

Example 15: Transfection of HepG2 Cells with psHBV-1 and Nucleic acid

The human hepatocellular carcinoma cell line Hep G2 was grown in Dulbecco's modified Eagle media supplemented with 10% fetal calf serum, 2 mM glutamine, 0.1 mM nonessential amino acids, 1 mM sodium pyruvate, 25 mM Hepes, 100 units penicillin, and 100 µg/ml streptomycin. To generate a replication competent cDNA, prior to transfection the HBV genomic sequences are excised from the bacterial plasmid sequence contained in the psHBV-1 vector. This was done with an EcoRI and Hind III restriction digest. Following completion of the digest, a ligation was performed under dilute conditions (20 µg/ml) to favor intermolecular ligation. The total ligation mixture was then concentrated using Qiagen spin columns. One skilled in the art would realize that other methods can be used to generate a replication competent cDNA.

Secreted alkaline phosphatase (SEAP) was used to normalize the HBsAg levels to control for transfection variability. The pSEAP2-TK control vector was constructed by ligating a Bgl II-Hind III fragment of the pRL-TK vector (Promega), containing the herpes simplex virus thymidine kinase promoter region, into Bgl II/Hind III digested pSEAP2-Basic (Clontech). Hep G2 cells were plated (3×10^4 cells/well) in 96-well microtiter plates and incubated overnight. A lipid/DNA/nucleic acid complex was formed containing (at final concentrations) cationic lipid (15 µg/ml), prepared psHBV-1 (4.5 µg/ml), pSEAP2-TK (0.5 µg/ml), and nucleic acid (100 µM). Following a 15 min. incubation at 37° C, the complexes were added to the plated Hep G2 cells. Media was removed from the cells 96 hr. post-transfection for HBsAg and SEAP analysis.

Transfection of the human hepatocellular carcinoma cell line, Hep G2, with replication competent HBV DNA results in the expression of HBV proteins and the production of virions.

Example 16: Analysis of HBsAg and SEAP Levels Following Nucleic Acid Treatment

Immulon 4 (Dynax) microtiter wells were coated overnight at 4° C with anti-HBsAg Mab (Biostride B88-95-31ad,ay) at 1 µg/ml in Carbonate Buffer (Na₂CO₃ 15 mM, NaHCO₃ 35 mM, pH 9.5). The wells were then washed 4x with PBST (PBS, 0.05% Tween® 20) and blocked for 1 hr at 37° C with PBST, 1% BSA. Following washing as above, the wells were dried at 37° C for 30 min. Biotinylated goat anti-HBsAg (Accurate YVS1807) was diluted 1:1000 in PBST and incubated in the wells for 1 hr. at 37° C. The wells were washed 4x with PBST. Streptavidin/Alkaline Phosphatase Conjugate (Pierce 21324) was diluted to 250

ng/ml in PBST, and incubated in the wells for 1 hr. at 37° C. After washing as above, p-nitrophenyl phosphate substrate (Pierce 37620) was added to the wells, which were then incubated for 1 hr. at 37° C. The optical density at 405 nm was then determined. SEAP levels were assayed using the Great EscAPe® Detection Kit (Clontech K2041-1), as per the manufacturers instructions.

Example 17: Analysis of HBV DNA expression a HepG2.2.15 murine model

The development of new antiviral agents for the treatment of chronic Hepatitis B has been aided by the use of animal models that are permissive to replication of related Hepadnaviridae such as Woodchuck Hepatitis Virus (WHV) and Duck Hepatitis Virus (DHV). In addition, the use of transgenic mice has also been employed. The human hepatoblastoma cell line, HepG2.2.15, implanted as a subcutaneous (SC) tumor, can be used to produce Hepatitis B viremia in mice. This model is useful for evaluating new HBV therapies. Mice bearing HepG2.2.15 SC tumors show HBV viremia. HBV DNA can be detected in serum beginning on Day 35. Maximum serum viral levels reach 1.9×10^5 copies/mL by day 49. A study also determined that the minimum tumor volume associated with viremia was 300 mm³. Therefore, the HepG2.2.15 cell line grown as a SC tumor produces a useful model of HBV viremia in mice. This new model can be suitable for evaluating new therapeutic regimens for chronic Hepatitis B.

HepG2.2.15 tumor cells contain a slightly truncated version of viral HBV DNA and sheds HBV particles. The purpose of this study was to identify what time period viral particles are shed from the tumor. Serum was analyzed for presence of HBV DNA over a time course after HepG2.2.15 tumor inoculation in Athymic Ncr nu/nu mice. HepG2.2.15 cells were carried and expanded in DMEM/10% FBS/2.4% HEPES/1% NEAA/1% Glutamine/1% Sodium Pyruvate media. Cells were resuspended in Delbecco's PBS with calcium/magnesium for injection. One hundred microliters of the tumor cell suspension (at a concentration of 1×10^8 cells/mL) were injected subcutaneously in the flank of NCR nu/nu female mice with a 23g1 needle and 1 cc syringe, thereby giving each mouse 1×10^7 cells. Tumors were allowed to grow for a period of up to 49 days post tumor cell inoculation. Serum was sampled for analysis on days 1, 7, 14, 35, 42 and 49 post tumor inoculation. Length and width measurements from each tumor were obtained three times per week using a Jamison microcaliper. Tumor volumes were calculated from tumor length/width measurements (tumor volume = $0.5[a(b)^2]$ where a = longest axis of the tumor and b = shortest axis of the tumor). Serum was analyzed for the presence of HBV DNA by the Roche Amplicor HBV monitor TM DNA assay.

Experiment 1

HepG2.2.15 cells were carried and expanded in DMEM/10% FBS/2.4%HEPES/1%NEAA/1% Glutamine/1% Sodium Pyruvate media. Cells were resuspended in Delbecco's PBS with calcium/magnesium for injection. One hundred microliters of the tumor cell suspension (at a concentration of 1×10^8 cells/mL) were injected subcutaneously in the flank of NCR nu/nu female mice with a 23g1 needle and 1 cc syringe, thereby giving each mouse 1×10^7 cells. Tumors were allowed to grow for a period of up to 49 days post tumor cell inoculation. Serum was sampled for analysis on days 1, 7, 14, 35, 42 and 49 post tumor inoculation. Length and width measurements from each tumor were obtained three times per week using a Jamison microcaliper. Tumor volumes were calculated from tumor length/width measurements (tumor volume = $0.5[a(b)^2]$ where a = longest axis of the tumor and b = shortest axis of the tumor). Serum was analyzed for the presence of HBV DNA by the Roche Amplicor HBV monitor TM DNA assay.

Results

When athymic nu/nu female mice are subcutaneously injected with HepG2.2.15 cells and form tumors, HBV DNA is detected in serum (peak serum level was 1.9×10^5 copies/mL). There is a positive correlation ($r_s = 0.7$, $p < 0.01$) between tumor weight (milligrams) and HB viral copies/mL serum. **Figure 21** shows a plot of HepG2.2.15 tumors in nu/nu female mice as tumor volume vs time. **Table XVI** shows the concentration of HBV DNA in relation to tumor size in the HepG2.2.15 implanted nu/nu female mice used in the study.

Experiment 2

HepG2.2.15 cells were carried and expanded in DMEM/10% FBS/2.4%HEPES/1%NEAA/1% Glutamine/1% Sodium Pyruvate media containing 400 µg/ml G418 antibiotic. G418-resistant cells were resuspended in Dulbecco's PBS with calcium/magnesium for injection. One hundred microliters of the tumor cell suspension (at a concentration of 1×10^8 cells/mL) were injected subcutaneously in the flank of NCR nu/nu female mice with a 23g1 needle and 1 cc syringe, thereby giving each mouse 1×10^7 cells. Tumors were allowed to grow for a period of up to 49 days post tumor cell inoculation. Serum was sampled for analysis on day 37 post tumor inoculation. Length and width measurements from each tumor were obtained three times per week using a Jamison microcaliper. Tumor volumes were calculated from tumor length/width measurements (tumor volume = $0.5[a(b)^2]$ where a = longest axis of the tumor and b = shortest axis of the tumor). Serum was analyzed for the presence of HBV DNA by the Roche Amplicor HBV monitor TM DNA assay.

Results

When athymic nu/nu female mice are subcutaneously injected with G418 antibiotic resistant HepG2.2.15 cells and form tumors, HBV DNA is detected in serum (peak serum level was 4.0×10^5 copies/mL). There is a positive correlation ($r_s = 0.7$, $p < 0.01$) between tumor weight (milligrams) and HB viral copies/mL serum. **Figure 22** shows a plot of HepG2.2.15 tumors in nu/nu female mice as tumor volume vs time. **Table XVII** shows the concentration of HBV DNA in relation to tumor size in the G418 antibiotic resistant HepG2.2.15 implanted nu/nu female mice used in the study.

Example 18: Identification of Potential Enzymatic nucleic acid molecules Cleavage Sites in HCV RNA

The sequence of HCV RNA was screened for accessible sites using a computer folding algorithm. Regions of the mRNA that did not form secondary folding structures and contained potential enzymatic nucleic acid cleavage sites were identified. The sequences of these cleavage sites are shown in **Tables XVIII, XIX, XX and XXIII**.

Example 19: Selection of Enzymatic nucleic acid molecules Cleavage Sites in HCV RNA

Enzymatic nucleic acid target sites were chosen by analyzing sequences of Human HCV (Genbank accession Nos: D11168, D50483.1, L38318 and S82227) and prioritizing the sites on the basis of folding. Enzymatic nucleic acid molecules are designed that could bind each target and are individually analyzed by computer folding (Christoffersen *et al.*, 1994 *J. Mol. Struct. Theochem*, 311, 273; Jaeger *et al.*, 1989, *Proc. Natl. Acad. Sci. USA*, 86, 7706) to assess whether the enzymatic nucleic acid molecules sequences fold into the appropriate secondary structure. Those enzymatic nucleic acid molecules with unfavorable intramolecular interactions between the binding arms and the catalytic core can be eliminated from consideration. As noted below, varying binding arm lengths can be chosen to optimize activity. Generally, at least 4 bases on each arm are able to bind to, or otherwise interact with, the target RNA.

Example 20: Chemical Synthesis and Purification of Enzymatic nucleic acids

Enzymatic nucleic acid molecules can be designed to anneal to various sites in the RNA message. The binding arms of the enzymatic nucleic acid molecules are complementary to the target site sequences described above. The enzymatic nucleic acid molecules can be chemically synthesized using, for example, RNA syntheses such as those described above and those described in Usman *et al.*, (1987 *J. Am. Chem. Soc.*, 109, 7845), Scaringe *et al.*, (1990 *Nucleic Acids Res.*, 18, 5433) and Wincott *et al.*, *supra*. Such methods make use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. The average stepwise coupling yields are

typically >98%. Enzymatic nucleic acid molecules can be modified to enhance stability by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-fluoro, 2'-O-methyl, 2'-H (for a review see Usman and Cedergren, 1992 TIBS 17, 34).

Enzymatic nucleic acid molecules can also be synthesized from DNA templates using bacteriophage T7 RNA polymerase (Milligan and Uhlenbeck, 1989, Methods Enzymol. 180, 51). Enzymatic nucleic acid molecules can be purified by gel electrophoresis using known methods, or can be purified by high pressure liquid chromatography (HPLC; See Wincott et al., supra; the totality of which is hereby incorporated herein by reference), and are resuspended in water. The sequences of chemically synthesized enzymatic nucleic acid constructs are shown below in **Tables XX, XXI and XXIII**. The antisense nucleic acid molecules shown in **Table XXII** were chemically synthesized.

Inactive enzymatic nucleic acid molecules, for example inactive hammerhead enzymatic nucleic acids, can be synthesized by substituting the order of G5A6 and substituting a U for A14 (numbering from Hertel et al., 1992 Nucleic Acids Res., 20, 3252).

Example 21: Enzymatic Nucleic Acid Cleavage of HCV RNA Target *in vitro*

Enzymatic nucleic acid molecules targeted to the HCV are designed and synthesized as described above. These enzymatic nucleic acid molecules can be tested for cleavage activity *in vitro*, for example using the following procedure. The target sequences and the nucleotide location within the HCV are given in **Tables XVIII, XIX, XX and XXIII**.

Cleavage Reactions: Full-length or partially full-length, internally-labeled target RNA for enzymatic nucleic acid molecule cleavage assay is prepared by *in vitro* transcription in the presence of [α -³²P] CTP, passed over a G 50 Sephadex column by spin chromatography and used as substrate RNA without further purification. Alternately, substrates are 5'-³²P-end labeled using T4 polynucleotide kinase enzyme. Assays are performed by pre-warming a 2X concentration of purified enzymatic nucleic acid molecule in enzymatic nucleic acid molecule cleavage buffer (50 mM Tris-HCl, pH 7.5 at 37°C; 10 mM MgCl₂) and the cleavage reaction was initiated by adding the 2X enzymatic nucleic acid molecule mix to an equal volume of substrate RNA (maximum of 1-5 nM) that was also pre-warmed in cleavage buffer. As an initial screen, assays are carried out for 1 hour at 37°C using a final concentration of either 40 nM or 1 mM enzymatic nucleic acid molecule, *i.e.*, enzymatic nucleic acid molecule excess. The reaction is quenched by the addition of an equal volume of 95% formamide, 20 mM EDTA, 0.05% bromophenol blue and 0.05% xylene cyanol after which the sample is heated to 95°C for 2 minutes, quick chilled and loaded onto a denaturing polyacrylamide gel. Substrate RNA and the specific RNA cleavage products generated by enzymatic nucleic acid molecule cleavage are visualized on an autoradiograph of the gel. The

percentage of cleavage is determined by Phosphor Imager[®] quantitation of bands representing the intact substrate and the cleavage products.

Alternatively, enzymatic nucleic acid molecules and substrates were synthesized in 96-well format using 0.2 μ mol scale. Substrates were 5'-³²P labeled and gel purified using 7.5% polyacrylamide gels, and eluting into water. Assays were done by combining trace substrate with 500nM enzymatic nucleic acid or greater, and initiated by adding final concentrations of 40mM Mg⁺², and 50mM Tris-Cl pH 8.0. For each enzymatic nucleic acid/substrate combination a control reaction was done to ensure cleavage was not the result of non-specific substrate degradation. A single three hour time point was taken and run on a 15% polyacrylamide gel to assess cleavage activity. Gels were dried and scanned using a Molecular Dynamics Phosphorimager and quantified using Molecular Dynamics ImageQuant software. Percent cleaved was determined by dividing values for cleaved substrate bands by full-length (uncleaved) values plus cleaved values and multiplying by 100 (%cleaved=[C/(U+C)]*100). In vitro cleavage data of enzymatic nucleic acid molecules targeting plus and minus strand HCV RNA is shown in **Table XXIII**.

Example 22: Inhibition of Luciferase Activity Using HCV Targeting Enzymatic nucleic acids in OST7 Cells

The capability of enzymatic nucleic acids to inhibit HCV RNA intracellularly was tested using a dual reporter system that utilizes both firefly and Renilla luciferase (**Figure 23**). The enzymatic nucleic acids targeted to the 5' HCV UTR region, which when cleaved, would prevent the translation of the transcript into luciferase.

Synthesis of Stabilized Enzymatic nucleic acids

Enzymatic nucleic acids were designed to target 15 sites within the 5'UTR of the HCV RNA (**Figure 24**) and synthesized as previously described, except that all enzymatic nucleic acids contain two 2'-amino uridines. Enzymatic nucleic acid and paired control sequences for targeted sites used in various examples herein are shown in **Table XXI**.

Reporter plasmids

The T7/HCV/firefly luciferase plasmid (HCVT7C₁₋₃₄₁, genotype 1a) was graciously provided by Aleem Siddiqui (University of Colorado Health Sciences Center, Denver, CO). The T7/HCV/firefly luciferase plasmid contains a T7 bacteriophage promoter upstream of the HCV 5'UTR (nucleotides 1-341)/firefly luciferase fusion DNA. The Renilla luciferase control plasmid (pRLSV40) was purchased from PROMEGA.

Luciferase assay

Dual luciferase assays were carried out according to the manufacturer's instructions (PROMEGA) at 4 hours after co-transfection of reporter plasmids and enzymatic nucleic acids. All data is shown as the average ratio of HCV/firefly luciferase luminescence over Renilla luciferase luminescence as determined by triplicate samples \pm SD.

Cell culture and transfections

OST7 cells were maintained in Dulbecco's modified Eagle's medium (GIBCO BRL) supplemented with 10% fetal calf serum, L-glutamine (2 mM) and penicillin/streptomycin. For transfections, OST7 cells were seeded in black-walled 96-well plates (Packard) at a density of 12,500 cells/well and incubated at 37°C under 5% CO₂ for 24 hours. Co-transfection of target reporter HCV7C (0.8 μ g/mL), control reporter pRLSV40, (1.2 μ g/mL) and enzymatic nucleic acid, (50 - 200 nM) was achieved by the following method: a 5X mixture of HCV7C (4 μ g/mL), pRLSV40 (6 μ g/mL) enzymatic nucleic acid (250 - 1000 nM) and cationic lipid (28.5 μ g/mL) was made in 150 μ L of OPTI-MEM (GIBCO BRL) minus serum. Reporter/enzymatic nucleic acid/lipid complexes were allowed to form for 20 min at 37°C under 5% CO₂. Medium was aspirated from OST7 cells and replaced with 120 μ L of OPTI-MEM (GIBCO BRL) minus serum, immediately followed by the addition of 30 μ L of 5X reporter/enzymatic nucleic acid/lipid complexes. Cells were incubated with complexes for 4 hours at 37°C under 5% CO₂.

IC₅₀ determinations for dose response curves

Apparent IC₅₀ values were calculated by linear interpolation. The apparent IC₅₀ is 1/2 the maximal response between the two consecutive points in which approximately 50% inhibition of HCV/luciferase expression is observed on the dose curve.

Quantitation of RNA Samples

Total RNA from transfected cells was purified using the Qiagen RNeasy 96 procedure including a DNase I treatment according to the manufacturer's instructions. Real time RT-PCR (Taqman assay) was performed on purified RNA samples using separate primer/probe sets specific for either firefly or Renilla luciferase RNA. Firefly luciferase primers and probe were upper (5'-CGGTCGGTAAAGTTGTTCCATT-3') (SEQ ID NO. 16202), lower (5'-CCTCTGACACATAATTCGCCTCT-3') (SEQ ID NO. 16203), and probe (5'-FAM-TGAAGCGAAGGTTGTGGATCTGGATACC-TAMRA-3') (SEQ ID NO 16204), and Renilla luciferase primers and probe were upper (5'-GTTTATTGAATCGGACCCAGGAT-3') (SEQ ID NO. 16205), lower (5'-AGGTGCATCTTCTTGCAGAAA-3') (SEQ ID NO. 16206), and probe (5'-FAM-CTTTTCCAATGCTATTGTTGAAGGTGCCAA-3') (SEQ ID NO. 16207) -TAMRA, both sets of primers and probes were purchased from Integrated DNA

Technologies. RNA levels were determined from a standard curve of amplified RNA purified from a large-scale transfection. RT minus controls established that RNA signals were generated from RNA and not residual plasmid DNA. RT-PCR conditions were: 30 min at 48°C, 10 min at 95°C, followed by 40 cycles of 15 sec at 95°C and 1 min at 60°C. Reactions were performed on an ABI Prism 7700 sequence detector. Levels of firefly luciferase RNA were normalized to the level of Renilla luciferase RNA present in the same sample. Results are shown as the average of triplicate treatments \pm SD.

Example 23: Inhibition of HCV 5'UTR-luciferase expression by synthetic stabilized enzymatic nucleic acids

The primary sequence of the HCV 5'UTR and characteristic secondary structure (Figure 24) is highly conserved across all HCV genotypes, thus making it a very attractive target for enzymatic nucleic acid-mediated cleavage. Enzymatic hammerhead nucleic acids, as a generally shown in Figure 25 and Table XXI (RPI 12249-12254, 12257-12265) were designed and synthesized to target 15 of the most highly conserved sites in the 5'UTR of HCV RNA. These synthetic enzymatic nucleic acids were stabilized against nuclease degradation by the addition of modifications such as 2'-O-methyl nucleotides, 2'-amino-uridines at U4 and U7 core positions, phosphorothioate linkages, and a 3'-inverted abasic cap.

In order to mimic cytoplasmic transcription of the HCV genome, OST7 cells were transfected with a target reporter plasmid containing a T7 bacteriophage promoter upstream of a HCV 5'UTR/firefly luciferase fusion gene. Cytoplasmic expression of the target reporter is facilitated by high levels of T7 polymerase expressed in the cytoplasm of OST7 cells. Co-transfection of target reporter HCVT7C₁₋₃₄₁ (firefly luciferase), control reporter pRLSV40 (Renilla luciferase) and enzymatic nucleic acid was carried out in the presence of cationic lipid. To determine the background level of luciferase activity, applicant used a control enzymatic nucleic acid that targets an irrelevant, non-HCV sequence. Transfection of reporter plasmids in the presence of this irrelevant control enzymatic nucleic acid (ICR) resulted in a slight decrease of reporter expression when compared to transfection of reporter plasmids alone. Therefore, the ICR was used to control for non-specific effects on reporter expression during treatment with HCV specific enzymatic nucleic acids. Renilla luciferase expression from the pRLSV40 reporter was used to normalize for transfection efficiency and sample recovery.

Of the 15 amino-modified hammerhead enzymatic nucleic acids tested, 12 significantly inhibited HCV/luciferase expression ($> 45\%$, $P < 0.05$) as compared to the ICR (Figure 26A). These data suggest that most of the HCV 5'UTR sites targeted here are accessible to enzymatic nucleic acid binding and subsequent RNA cleavage. To investigate further the

enzymatic nucleic acid-dependent inhibition of HCV/luciferase activity, hammerhead enzymatic nucleic acids designed to cleave after sites 79, 81, 142, 192, 195, 282 or 330 of the HCV 5'UTR were selected for continued study because their anti-HCV activity was the most efficacious over several experiments. A corresponding attenuated core (AC) control was synthesized for each of the 7 active enzymatic nucleic acids (Table XX). Each paired AC control contains similar nucleotide composition to that of its corresponding active enzymatic nucleic acid however, due to scrambled binding arms and changes to the catalytic core, lacks the ability to bind or catalyze the cleavage of HCV RNA. Treatment of OST7 cells with enzymatic nucleic acids designed to cleave after sites 79, 81, 142, 195 or 330 resulted in significant inhibition of HCV/luciferase expression (65%, 50%, 50%, 80% and 80%, respectively) when compared to HCV/luciferase expression in cells treated with corresponding ACs, $P < 0.05$ (Figure 26B). It should be noted that treatment with either the ICR or ACs for sites 79, 81, 142 or 192 caused a greater reduction of HCV/luciferase expression than treatment with ACs for sites 195, 282 or 330. The observed differences in HCV/luciferase expression after treatment with ACs most likely represents the range of activity due to non-specific effects of oligonucleotide treatment and/or differences in base composition. Regardless of differences in HCV/luciferase expression levels observed as a result of treatment with ACs, active enzymatic nucleic acids designed to cleave after sites 79, 81, 142, 195, or 330 demonstrated similar and potent anti-HCV activity (Figure 26B).

Example 24: Synthetic stabilized enzymatic nucleic acids inhibit HCV/luciferase expression in a concentration-dependent manner

In order to characterize enzymatic nucleic acid efficacy in greater detail, these same 5 lead hammerhead enzymatic nucleic acids were tested for their ability to inhibit HCV/luciferase expression over a range of enzymatic nucleic acid concentrations (0 nM - 100 nM). For constant transfection conditions, the total concentration of nucleic acid was maintained at 100 nM for all samples by mixing the active enzymatic nucleic acid with its corresponding AC. Moreover, mixing of active enzymatic nucleic acid and AC maintains the lipid to nucleic acid charge ratio. A concentration-dependent inhibition of HCV/luciferase expression was observed after treatment with each of the 5 enzymatic nucleic acids (Figures 27A-E). By linear interpolation, the enzymatic nucleic acid concentration resulting in 50% inhibition (apparent IC_{50}) of HCV/luciferase expression ranged from 40 - 215 nM. The two most efficacious enzymatic nucleic acids were those designed to cleave after sites 195 or 330 with apparent IC_{50} values of 46 nM and 40 nM, respectively (Figures 27D and E).

Example 25: An enzymatic nucleic acid mechanism is required for the observed inhibition of HCV/luciferase expression

To confirm that an enzymatic nucleic acid mechanism of action was responsible for the observed inhibition of HCV/luciferase expression, paired binding-arm attenuated core (BAC) controls (RPI 15291 and 15294) were synthesized for direct comparison to enzymatic nucleic acids targeting sites 195 (RPI 12252) and 330 (RPI 12254). Paired BACs can specifically bind HCV RNA but are unable to promote RNA cleavage because of changes in the catalytic core and, thus, can be used to assess inhibition due to binding alone. Also included in this comparison were paired SAC controls (RPI 15292 and 15295) that contain scrambled binding arms and attenuated catalytic cores, and so lack the ability to bind the target RNA or to catalyze target RNA cleavage.

Enzymatic nucleic acid cleavage of target RNA should result in both a lower level of HCV/luciferase RNA and a subsequent decrease in HCV/luciferase expression. In order to analyze target RNA levels, a reverse transcriptase/polymerase chain reaction (RT-PCR) assay was employed to quantify HCV/luciferase RNA levels. Primers were designed to amplify the luciferase coding region of the HCV 5'UTR/luciferase RNA. This region was chosen because HCV-targeted enzymatic nucleic acids that might co-purify with cellular RNA would not interfere with RT-PCR amplification of the luciferase RNA region. Primers were also designed to amplify the Renilla luciferase RNA so that Renilla RNA levels could be used to control for transfection efficiency and sample recovery.

OST7 cells were treated with active enzymatic nucleic acids designed to cleave after sites 195 or 330, paired SACs, or paired BACs. Treatment with enzymatic nucleic acids targeting site 195 or 330 resulted in a significant reduction of HCV/luciferase RNA when compared to their paired SAC controls ($P < 0.01$). In this experiment the site 195 enzymatic nucleic acid was more efficacious than the site 330 enzymatic nucleic acid (Figure 28A). Treatment with paired BACs that target site 195 or 330 did not reduce HCV/luciferase RNA when compared to the corresponding SACs, thus confirming that the ability to bind alone does not result in a reduction of HCV/luciferase RNA.

To confirm that enzymatic nucleic acid-mediated cleavage of target RNA is necessary for inhibition of HCV/luciferase expression, HCV/luciferase activity was determined in the same experiment. As expected, significant inhibition of HCV/luciferase expression was observed after treatment with active enzymatic nucleic acids when compared to paired SACs (Figure 28B). Importantly, treatment with paired BACs did not inhibit HCV/luciferase expression, thus confirming that the ability to bind alone is also not sufficient to inhibit translation. As observed in the RNA assay, the site 195 enzymatic nucleic acid was more efficacious than the site 330 enzymatic nucleic acid in this experiment. However, a correlation between enzymatic nucleic acid-mediated HCV RNA reduction and inhibition of HCV/luciferase translation was observed for enzymatic nucleic acids to both sites. The

reduction in target RNA and the necessity for an active enzymatic nucleic acid catalytic core confirm that a enzymatic nucleic acid mechanism is required for the observed reduction in HCV/luciferase protein activity in cells treated with site 195 or site 330 enzymatic nucleic acids.

Example 26: Zinzyme Inhibition of chimeric HCV/Poliovirus replication

During HCV infection, viral RNA is present as a potential target for enzymatic nucleic acid cleavage at several processes: un-coating, translation, RNA replication and packaging. Target RNA can be more or less accessible to enzymatic nucleic acid cleavage at any one of these steps. Although the association between the HCV initial ribosome entry site (IRES) and the translation apparatus is mimicked in the HCV 5'UTR/luciferase reporter system, these other viral processes are not represented in the OST7 system. The resulting RNA/protein complexes associated with the target viral RNA are also absent. Moreover, these processes can be coupled in an HCV-infected cell which could further impact target RNA accessibility. Therefore, applicant tested whether enzymatic nucleic acids designed to cleave the HCV 5'UTR could effect a replicating viral system.

Recently, Lu and Wimmer characterized a HCV-poliovirus chimera in which the poliovirus IRES was replaced by the IRES from HCV (Lu & Wimmer, 1996, Proc. Natl. Acad. Sci. USA. 93, 1412-1417). Poliovirus (PV) is a positive strand RNA virus like HCV, but unlike HCV is non-enveloped and replicates efficiently in cell culture. The HCV-PV chimera expresses a stable, small plaque phenotype relative to wild type PV.

The following enzymatic nucleic acid molecules (zinzymes) were synthesized and tested for replicative inhibition of an HCV/Poliovirus chimera: RPI 18763, RPI 18812, RPI 18749, RPI 18765, RPI 18792, and RPI 18814 (Table XX). A scrambled attenuated core enzymatic nucleic acid, RPI 18743, was used as a control.

HeLa cells were infected with the HCV-PV chimera for 30 minutes and immediately treated with enzymatic nucleic acid. HeLa cells were seeded in U-bottom 96-well plates at a density of 9000-10,000 cells/well and incubated at 37°C under 5% CO₂ for 24 h. Transfection of nucleic acid (200 nM) was achieved by mixing of 10X nucleic acid (2000 nM) and 10X of a cationic lipid (80 µg/ml) in DMEM (Gibco BRL) with 5% fetal bovine serum (FBS). Nucleic acid/lipid complexes were allowed to incubate for 15 minutes at 37°C under 5% CO₂. Medium was aspirated from cells and replaced with 80 µl of DMEM (Gibco BRL) with 5% FBS serum, followed by the addition of 20 µl of 10X complexes. Cells were incubated with complexes for 24 hours at 37°C under 5% CO₂.

The yield of HCV-PV from treated cells was quantified by plaque assay. The plaque assays were performed by diluting virus samples in serum-free DMEM (Gibco BRL) and applying 100 μ l to HeLa cell monolayers (~80% confluent) in 6-well plates for 30 minutes. Infected monolayers were overlaid with 3 ml 1.2% agar (Sigma) and incubated at 37°C under 5% CO₂. Two or three days later the overlay was removed, monolayers were stained with 1.2% crystal violet, and plaque forming units were counted. The results for the zinc finger inhibition of HCV-PV replication are shown in **Figure 33**.

Example 27: Antisense inhibition of chimeric HCV/Poliovirus replication

Antisense nucleic acid molecules (RPI 17501 and RPI 17498, **Table XXII**) were tested for replicative inhibition of an HCV/Poliovirus chimera compared to scrambled controls. An antisense nucleic acid molecule is a non-enzymatic nucleic acid molecule that binds to target RNA by means of RNA-RNA or RNA-DNA or RNA-PNA (protein nucleic acid; Egholm et al., 1993 Nature 365, 566) interactions and alters the activity of the target RNA (for a review, see Stein and Cheng, 1993 Science 261, 1004 and Woolf et al., US patent No. 5,849,902). Typically, antisense molecules are complementary to a target sequence along a single contiguous sequence of the antisense molecule. However, in certain embodiments, an antisense molecule can bind to substrate such that the substrate molecule forms a loop, and/or an antisense molecule can bind such that the antisense molecule forms a loop. Thus, the antisense molecule can be complementary to two (or even more) non-contiguous substrate sequences or two (or even more) non-contiguous sequence portions of an antisense molecule can be complementary to a target sequence or both. For a review of current antisense strategies, see Schmajuk et al., 1999, J. Biol. Chem., 274, 21783-21789, Delihias et al., 1997, Nature, 15, 751-753, Stein et al., 1997, Antisense N. A. Drug Dev., 7, 151, Crooke, 2000, Methods Enzymol., 313, 3-45; Crooke, 1998, Biotech. Genet. Eng. Rev., 15, 121-157, Crooke, 1997, Ad. Pharmacol., 40, 1-49. In addition, antisense DNA can be used to target RNA by means of DNA-RNA interactions, thereby activating RNase H, which digests the target RNA in the duplex. The antisense oligonucleotides can comprise one or more RNase H activating region, which is capable of activating RNase H cleavage of a target RNA. Antisense DNA can be synthesized chemically or expressed via the use of a single stranded DNA expression vector or equivalent thereof. Additionally, antisense molecules can be used in combination with the enzymatic nucleic acid molecules of the instant invention.

A RNase H activating region is a region (generally greater than or equal to 4-25 nucleotides in length, preferably from 5-11 nucleotides in length) of a nucleic acid molecule capable of binding to a target RNA to form a non-covalent complex that is recognized by cellular RNase H enzyme (see for example Arrow et al., US 5,849,902; Arrow et al., US 5,989,912). The RNase H enzyme binds to the nucleic acid molecule-target RNA complex

and cleaves the target RNA sequence. The RNase H activating region comprises, for example, phosphodiester, phosphorothioate (preferably at least four of the nucleotides are phosphorothioate substitutions; more specifically, 4-11 of the nucleotides are phosphorothioate substitutions); phosphorodithioate, 5'-thiophosphate, or methylphosphonate backbone chemistry or a combination thereof. In addition to one or more backbone chemistries described above, the RNase H activating region can also comprise a variety of sugar chemistries. For example, the RNase H activating region can comprise deoxyribose, arabinose, fluoroarabinose or a combination thereof, nucleotide sugar chemistry. Those skilled in the art will recognize that the foregoing are non-limiting examples and that any combination of phosphate, sugar and base chemistry of a nucleic acid that supports the activity of RNase H enzyme is within the scope of the definition of the RNase H activating region and the instant invention.

HeLa cells were infected with the HCV-PV chimera for 30 minutes and immediately treated with antisense nucleic acid. HeLa cells were seeded in U-bottom 96-well plates at a density of 9000-10,000 cells/well and incubated at 37°C under 5% CO₂ for 24 h. Transfection of nucleic acid (200 nM) was achieved by mixing of 10X nucleic acid (2000 nM) and 10X of a cationic lipid (80 µg/ml) in DMEM (Gibco BRL) with 5% fetal bovine serum (FBS). Nucleic acid/lipid complexes were allowed to incubate for 15 minutes at 37°C under 5% CO₂. Medium was aspirated from cells and replaced with 80 µl of DMEM (Gibco BRL) with 5% FBS serum, followed by the addition of 20 µls of 10X complexes. Cells were incubated with complexes for 24 hours at 37°C under 5% CO₂.

The yield of HCV-PV from treated cells was quantified by plaque assay. The plaque assays were performed by diluting virus samples in serum-free DMEM (Gibco BRL) and applying 100 µl to HeLa cell monolayers (~80% confluent) in 6-well plates for 30 minutes. Infected monolayers were overlaid with 3 ml 1.2% agar (Sigma) and incubated at 37°C under 5% CO₂. Two or three days later the overlay was removed, monolayers were stained with 1.2% crystal violet, and plaque forming units were counted. The results for the antisense inhibition of HCV-PV are shown in Figure 34.

Example 28: Nucleic acid Inhibition of Chimeric HCV/PV in combination with Interferon

One of the limiting factors in interferon (IFN) therapy for chronic HCV are the toxic side effects associated with IFN. Applicant has reasoned that lowering the dose of IFN needed can reduce these side effects. Applicant has previously shown that enzymatic nucleic acid molecules targeting HCV RNA have a potent antiviral effect against replication of an HCV-poliovirus (PV) chimera (Macejak *et al.*, 2000, *Hepatology*, 31, 769-776). In order to determine if the antiviral effect of type 1 IFN could be improved by the addition of anti-HCV enzymatic nucleic acid treatment, a dose response (0 U/ml to 100 U/ml) with IFN alfa 2a or

IFN alfa 2b was performed in HeLa cells in combination with 200 nM site 195 anti-HCV enzymatic nucleic acid (RPI 13919) or enzymatic nucleic acid control (SAC) treatment. The SAC control (RPI 17894) is a scrambled binding arm, attenuated core version of the site 195 enzymatic nucleic acid (RPI 13919). IFN dose responses were performed with different pretreatment regimes to find the dynamic range of inhibition in this system. In these studies, HeLa cells were used instead of HepG2 because of more efficient enzymatic nucleic acid delivery (Macejak *et al.*, 2000, *Hepatology*, 31, 769-776).

Cells and Virus

HeLa cells were maintained in DMEM (BioWhittaker, Walkersville, MD) supplemented with 5% fetal bovine serum. A cloned DNA copy of the HCV-PV chimeric virus was a gift of Dr. Eckard Wimmer (NYU, Stony Brook, NY). An RNA version was generated by in vitro transcription and transfected into HeLa cells to produce infectious virus (Lu and Wimmer, 1996, *PNAS USA.*, 93, 1412-1417).

Enzymatic nucleic acid Synthesis

Nuclease resistant enzymatic nucleic acids and control oligonucleotides containing 2'-O-methyl-nucleotides, 2'-deoxy-2'-C-allyl uridine, a 3'-inverted abasic cap, and phosphorothioate linkages were chemically synthesized. The anti-HCV enzymatic nucleic acid (RPI 13919) targeting cleavage after nucleotide 195 of the 5' UTR of HCV is shown in Table XX. Attenuated core controls have nucleotide changes in the core sequence that greatly diminished the enzymatic nucleic acid's cleavage activity. The attenuated controls either contain scrambled binding arms (referred to as SAC, RPI 18743) or maintain binding arms (BAC, RPI 17894) capable of binding to the HCV RNA target.

Enzymatic nucleic acid Delivery

A cationic lipid was used as a cytofectin agent. HeLa cells were seeded in 96-well plates at a density of 9000-10,000 cells/well and incubated at 37°C under 5% CO₂ for 24 h. Transfection of enzymatic nucleic acid or control oligonucleotides (200 nM) was achieved by mixing 10X enzymatic nucleic acid or control oligonucleotides (2000 nM) with 10X RPI.9778 (80 µg/ml) in DMEM containing 5% fetal bovine serum (FBS) in U-bottom 96-well plates to make 5X complexes. Enzymatic nucleic acid/lipid complexes were allowed to incubate for 15 min at 37°C under 5% CO₂. Medium was aspirated from cells and replaced with 80 µl of DMEM (Gibco BRL) containing 5% FBS serum, followed by the addition of 20 µl of 5X complexes. Cells were incubated with complexes for 24 h at 37°C under 5% CO₂.

Interferon/Enzymatic nucleic acid Combination Treatment

Interferon alfa 2a (Roferon®) was purchased from Roche Bioscience (Palo Alto, CA). Interferon alfa 2b (Intron A®) was purchased from Schering-Plough Corporation (Madison, NJ). Consensus interferon (interferon-alfa-con 1) was a generous gift of Amgen, Inc. (Thousand Oaks, CA). For the basis of comparison, the manufacturers' specified units were used in the studies reported here; however, the manufacturers' unit definitions of these three IFN preparations are not necessarily the same. Nevertheless, since clinical dosing is based on the manufacturers' specified units, a direct comparison based on these units has relevance to clinical therapeutic indices. HeLa cells were seeded (10,000 cells per well) and incubated at 37°C under 5% CO₂ for 24 h. Cells were then pre-treated with interferon in complete media (DMEM + 5% FBS) for 4 h and then infected with HCV-PV at a multiplicity of infection (MOI) = 0.1 for 30 min. The viral inoculum was then removed and enzymatic nucleic acid or attenuated control (SAC or BAC) was delivered with the cytofectin formulation (8 µg/ml) in complete media for 24 h as described above. Where indicated for enzymatic nucleic acid dose response studies, active enzymatic nucleic acid was mixed with SAC to maintain a 200 nM total oligonucleotide concentration and the same lipid charge ratio. After 24 h, cells were lysed to release virus by three cycles of freeze/thaw. Virus was quantified by plaque assay and viral yield is reported as mean plaque forming units per ml (pfu/ml) + SD. All experiments were repeated at least twice and the trends in the results reported were reproducible. Significance levels (P values) were determined by the Student's test.

Plaque Assay

Virus samples were diluted in serum-free DMEM and 100 µl applied to Vero cell monolayers (~80% confluent) in 6-well plates for 30 min. Infected monolayers were overlaid with 3 ml 1.2% agar (Sigma Chemical Company, St. Louis, MO) and incubated at 37°C under 5% CO₂. When plaques were visible (after two to three days) the overlay was removed, monolayers were stained with 1.2% crystal violet, and plaque forming units were counted.

Results

As shown in **Figure 29A** and **29B**, treatment with the site 195 (RPI 13919) anti-HCV hammerhead enzymatic nucleic acid alone (0 U/ml IFN) resulted in viral replication that was dramatically reduced compared to SAC-treated cells (85%, $P < 0.01$). For both IFN alfa 2a (**Figure 29A**) or IFN alfa 2b (**Figure 29B**), treatment with 25 U/ml resulted in a ~90% inhibition of HCV-PV replication in SAC-treated cells as compared to cells treated with SAC alone ($p < 0.01$ for both observations). The maximal level of inhibition in SAC-treated cells (94%) was achieved by treatment with ≥ 50 U/ml of either IFN alfa 2a or IFN alfa 2b ($p < 0.01$ for both observations *versus* SAC alone). Maximal inhibition could however, be achieved by a 5-fold lower dose of IFN alfa 2a (10 U/ml) if enzymatic nucleic acid targeting site 195 in the 5' UTR of HCV RNA was given in combination (**Figure 29A**, $p < 0.01$). While the

additional effect of enzymatic nucleic acid treatment on IFN alfa 2b-treated cells at 10 U/ml was very slight, the combined effect with 25 U/ml IFN alfa 2b was greater in magnitude (**Figure 29B**). For both interferons tested, pretreatment with 25 U/ml in combination with 200 nM site 195 anti-HCV enzymatic nucleic acid resulted in an even greater level of inhibition of viral replication (>98%) compared to replication in cells treated with 200 nM SAC alone ($P<0.01$).

A dose response of the site 195 anti-HCV enzymatic nucleic acid was also performed in HeLa cells, either with or without 12.5 U/ml IFN alfa 2a or IFN alfa 2b pretreatment. As shown in **Figure 30**, enzymatic nucleic acid-mediated inhibition was dose-dependent and a significant inhibition of HCV-PV replication (>75% *versus* 0 nM enzymatic nucleic acid, $P<0.01$) could be achieved by treatment with ≥ 150 nM anti-HCV enzymatic nucleic acid alone (no IFN). However, in IFN-pretreated cells, the dose of anti-HCV enzymatic nucleic acid needed to achieve this level of inhibition was decreased 3-fold to 50 nM ($P<0.01$ *versus* 0 nM enzymatic nucleic acid). In comparison, treatment with the site 195 anti-HCV enzymatic nucleic acid alone at 50 nM resulted in only ~40% inhibition of virus replication. Pretreatment with IFN enhanced the antiviral effect of site 195 enzymatic nucleic acid at all enzymatic nucleic acid doses, compared to no IFN pretreatment.

Interferon-alfacon1, consensus IFN (CIFN), is another type 1 IFN that is used to treat chronic HCV. To determine if a similar enhancement can occur in CIFN-treated cells, a dose response with CIFN was performed in HeLa cells using 0 U/ml to 12.5 U/ml CIFN in combination with 200 nM site 195 anti-HCV enzymatic nucleic acid or SAC treatment (**Figure 31A**). Again, in the presence of the site 195 anti-HCV enzymatic nucleic acid alone, viral replication was dramatically reduced compared to SAC-treated cells. As shown in **Figure 31A**, treatment with 200 nM anti-HCV enzymatic nucleic acid alone significantly inhibited HCV-PV replication (90% *versus* SAC treatment, $P<0.01$). However, pretreatment with concentrations of CIFN from 1 U/ml to 12.5 U/ml in combination with 200 nM anti-HCV enzymatic nucleic acid resulted in even greater inhibition of viral replication (>98%) compared to replication in cells treated with 200 nM SAC alone ($P<0.01$). It is important to note that pretreatment with 1 U/ml CIFN in SAC-treated cells did not have a significant effect on HCV-poliovirus replication, but in the presence of enzymatic nucleic acid a significant inhibition of replication was observed (>98%, $P<0.01$). Thus, the dose of CIFN needed to achieve a >98% inhibition could be lowered to 1 U/ml in cells also treated with 200 nM site 195 anti-HCV enzymatic nucleic acid.

A dose response of site 195 anti-HCV enzymatic nucleic acid was then performed in HeLa cells, either with or without 12.5 U/ml CIFN pretreatment. As shown in **Figure 31B**, a significant inhibition of HCV-PV replication (>95% *versus* 0 nM enzymatic nucleic acid,

$P < 0.01$) could be achieved by treatment with ≥ 150 nM anti-HCV enzymatic nucleic acid alone. However, in CIFN-pretreated cells, the dose of anti-HCV enzymatic nucleic acid needed to achieve this level of inhibition was only 50 nM ($P < 0.01$). In comparison, treatment with the site 195 anti-HCV enzymatic nucleic acid alone at 50 nM resulted in ~50% inhibition of virus replication. Thus, as was seen with IFN alfa 2a and IFN alfa 2b, the dose of enzymatic nucleic acid could be reduced 3-fold in the presence of CIFN pretreatment to achieve a similar antiviral effect as enzymatic nucleic acid-treatment alone.

To further explore the combination of lower enzymatic nucleic acid concentration and CIFN, a dose response with 0 U/ml to 12.5 U/ml CIFN was subsequently performed in HeLa cells in combination with 50 nM site 195 anti-HCV enzymatic nucleic acid treatment. In multiple experiments, treatment with 50 nM anti-HCV enzymatic nucleic acid alone inhibited HCV-PV replication 50% – 81% compared to viral replication in SAC-treated cells. As for the experiment shown in **Figure 31A**, treatment with CIFN alone at 5 U/ml resulted in ~50% inhibition of viral replication. However, a four hour pretreatment with 5 U/ml CIFN followed by 50 nM anti-HCV enzymatic nucleic acid treatment resulted in 95% - 97% inhibition compared to SAC-treated cells ($P < 0.01$).

To demonstrate that the enhanced antiviral effect of CIFN and enzymatic nucleic acid combination treatment was dependent upon enzymatic nucleic acid cleavage activity, the effect of CIFN in combination with site 195 anti-HCV enzymatic nucleic acid versus the effect of CIFN in combination with a binding competent, attenuated core, control (BAC) was then compared. The BAC can still bind to its specific RNA target, but is greatly diminished in cleavage activity. Pretreatment with 12.5 U/ml CIFN reduced the viral yield ~90% (7-fold) in cells treated with BAC (compare CIFN versus BAC in **Figure 32**). Cells treated with 200 nM site 195 anti-HCV enzymatic nucleic acid alone produced ~95% (17-fold) less virus than BAC-treated cells (195 RZ BAC in **Figure 32**). The combination of CIFN pretreatment and 200 nM site 195 anti-HCV enzymatic nucleic acid results in an augmented >98% (300-fold) reduction in viral yield (CIFN+RZ versus control in **Figure 32**).

2'-5'-Oligoadenylate Inhibition of HCV

Type 1 Interferon is a key constituent of many effective treatment programs for chronic HCV infection. Treatment with type 1 interferon induces a number of genes and results in an antiviral state within the cell. One of the genes induced is 2', 5' oligoadenylate synthetase, an enzyme that synthesizes short 2', 5' oligoadenylate (2-5A) molecules. Nascent 2-5A subsequently activates a latent RNase, RNase L, which in turn nonspecifically degrades viral RNA. As described herein, ribozymes targeting HCV RNA that inhibit the replication of an HCV-poliovirus (HCV-PV) chimera in cell culture and have shown that this antiviral effect is

augmented if ribozyme is given in combination with type 1 interferon. In addition, the 2-5A component of the interferon response can also inhibit replication of the HCV-PV chimera.

The antiviral effect of anti-HCV ribozyme treatment is enhanced if type 1 interferon is given in combination. Interferon induces a number of gene products including 2',5' oligoadenylate (2-5A) synthetase, double-stranded RNA-activated protein kinase (PKR), and the Mx proteins. Mx proteins appear to interfere with nuclear transport of viral complexes and are not thought to play an inhibitory role in HCV infection. On the other hand, the additional 2-5A-mediated RNA degradation (via RNase L) and/or the inhibition of viral translation by PKR in interferon-treated cells can augment the ribozyme-mediated inhibition of HCV-PV replication.

To investigate the potential role of the 2-5A/RNase L pathway in this enhancement phenomenon, HCV-PV replication was analyzed in HeLa cells treated exogenously with chemically-synthesized analogs of 2-5A (**Figure 35**), alone and in combination with the anti-HCV ribozyme (RPI 13919). These results were compared to replication in cells treated with interferon and/or anti-HCV ribozyme. Anti-HCV ribozyme was transfected into cells with a cationic lipid. To control for nonspecific effects due to lipid-mediated transfection, a scrambled arm, attenuated core, oligonucleotide (SAC) (RPI 17894) was transfected for comparison. The SAC is the same base composition as the ribozyme but is greatly attenuated in catalytic activity due to changes in the core sequence and cannot bind specifically to the HCV sequence.

As shown in **Figure 36A**, HeLa cells pretreated with 10 U/ml consensus interferon for 4 hours prior to HCV-PV infection resulted in ~70% reduction of viral replication in SAC-treated cells. Similarly, HeLa cells treated with 100 nM anti-HCV ribozyme for 20 hours after infection resulted in an ~80% reduction in viral yield. This antiviral effect was enhanced to ~98% inhibition in HeLa cells pretreated with interferon for 4 hours before infection and then treated with anti-HCV ribozyme for 20 hours after infection. In parallel, a 2-5A compound (analog I, **Figure 35**) that was protected from nuclease digestion at the 3'-end with an inverted abasic moiety was tested. As shown in **Figure 36B**, treatment with 200 nM 2-5A analog I for 4 hours prior to HCV-PV infection only slightly inhibited HCV-PV replication (~20%) in SAC-treated cells. Moreover, the inhibition due to a 20 hour anti-HCV ribozyme treatment was not augmented with a 4 hour pretreatment of 2-5A in combination (compare third bar to fourth bar in **Figure 36B**).

There are several possible explanations why the chemically synthesized 2-5A analog was not able to completely activate RNase L. It is possible that the 2-5A analog was not sufficiently stable or that in this experiment the 4 hour pretreatment period was too short for RNase L activation. To test these possibilities, a 2-5A compound containing a 5'-terminal

thiophosphate (P=S) for added nuclease resistance, in addition to the 3'- abasic, was also included (analog II, Figure 35). In addition, a longer 2-5A treatment was used. In this experiment (Figure 37), HeLa cells were treated with 2-5A or 2-5A(P=S) for 20 hours after HCV-PV infection. Again, anti-HCV ribozyme treatment resulted in >80% inhibition. In contrast to the 20% inhibition of viral replication seen with a 4 hour 2-5A pretreatment, viral replication in cells treated with 2-5A analog I for 20 hours after HCV-PV infection was inhibited by ~70%. The P=S version (analog II) inhibited HCV-PV replication by ~35%. Thus, both 2-5A analogs used here are able to generate an antiviral effect, presumably through RNase L activation. The P=S version, although more resistant to 5' dephosphorylation, did not yield as great an anti-viral effect. It is possible that combination of the 5'-terminal thiophosphate together with the presence of a 3'-inverted abasic moiety can interfere with RNase L activation. Nevertheless, these results demonstrate potent anti-HCV activity by a nuclease-stabilized 2-5A analog.

The level of reduction in HCV-PV replication in cells treated with 2-5A analog I for 20 hours was similar to that in cells pretreated with consensus interferon for 4 hours. To determine if this expanded 2-5A treatment regimen would enhance anti-HCV ribozyme efficacy to the same degree as does the interferon pretreatment, HeLa cells infected with HCV-PV were treated with a combination of 2-5A and anti-HCV ribozyme for 20 hours after infection. In this experiment, a 200 nM treatment with anti-HCV ribozyme or 2-5A treatment alone inhibited viral replication by 88% or ~60%, respectively, compared to SAC treatment (Figure 38, left three bars). To maintain consistent transfection conditions but vary the concentration of anti-HCV ribozyme or 2-5A, anti-HCV ribozyme was mixed with the SAC to maintain a total dose of 200 nM. A 50 nM treatment with anti-HCV ribozyme inhibited HCV-PV replication by ~70% (solid middle bar). However, the amount of HCV-PV replication was not further reduced in cells treated with a combination of 50 nM anti-HCV ribozyme and 150 nM 2-5A (striped middle bar). Likewise, cells treated with 100 nM anti-HCV ribozyme inhibited HCV-PV replication by ~80% whether they were also treated with 100 nM of 2-5A or SAC (right two bars). In contrast, antiviral activity increased from 80% to 98% when 100 nM anti-HCV ribozyme was given in combination with interferon (Figure 36A). The reasons for the lack of additive or synergistic effects for the ribozyme/2-5A combination therapy is unclear at this time but can be due to that fact that both compounds have a similar mechanism of action (degradation of RNA). Further study is warranted to examine this possibility.

As a monotherapy, 2-5A treatment generates a similar inhibitory effect on HCV-poliovirus replication as does interferon treatment. If these results are maintained in HCV patients, treatment with 2-5A can not only be efficacious but can also generate less side

effects than those observed with interferon if the plethora of interferon-induced genes were not activated.

HBV Cell Culture Models

As previously mentioned, HBV does not infect cells in culture. However, transfection of HBV DNA (either as a head-to-tail dimer or as an "overlength" genome of >100%) into HuH7 or Hep G2 hepatocytes results in viral gene expression and production of HBV virions released into the media. Thus, HBV replication competent DNA are co-transfected with ribozymes in cell culture. Such an approach has been used to report intracellular ribozyme activity against HBV (zu Putlitz, *et al.*, 1999, *J. Virol.*, 73, 5381-5387, and Kim *et al.*, 1999, *Biochem. Biophys. Res. Commun.*, 257, 759-765). In addition, stable hepatocyte cell lines have been generated that express HBV. In these cells, only ribozyme need be delivered; however, performance of a delivery screen is required. Intracellular HBV gene expression can be assayed by a Taqman® assay for HBV RNA or by ELISA for HBV protein. Extracellular virus can be assayed by PCR for DNA or ELISA for protein. Antibodies are commercially available for HBV surface antigen and core protein. A secreted alkaline phosphatase expression plasmid can be used to normalize for differences in transfection efficiency and sample recovery.

HBV Animal Models

There are several small animal models to study HBV replication. One is the transplantation of HBV-infected liver tissue into irradiated mice. Viremia (as evidenced by measuring HBV DNA by PCR) is first detected 8 days after transplantation and peaks between 18 – 25 days (Ilan *et al.*, 1999, *Hepatology*, 29, 553-562).

Transgenic mice that express HBV have also been used as a model to evaluate potential anti-virals. HBV DNA is detectable in both liver and serum (Guidotti *et al.*, 1995, *J. Virology*, 69, 10, 6158-6169; Morrey *et al.*, 1999, *Antiviral Res.*, 42, 97-108).

An additional model is to establish subcutaneous tumors in nude mice with Hep G2 cells transfected with HBV. Tumors develop in about 2 weeks after inoculation and express HBV surface and core antigens. HBV DNA and surface antigen is also detected in the circulation of tumor-bearing mice (Yao *et al.*, 1996, *J. Viral Hepat.*, 3, 19-22).

In one embodiment, the invention features a mouse, for example a male or female mouse, implanted with HepG2.2.15 cells, wherein the mouse is susceptible to HBV infection and capable of sustaining HBV DNA expression. One embodiment of the invention provides a mouse implanted with HepG2.2.15 cells, wherein said mouse sustains the propagation of

HEPG2.2.15 cells and HBV production (see Macejak, US Provisional Patent Application No. 60/296,876).

Woodchuck hepatitis virus (WHV) is closely related to HBV in its virus structure, genetic organization, and mechanism of replication. As with HBV in humans, persistent WHV infection is common in natural woodchuck populations and is associated with chronic hepatitis and hepatocellular carcinoma (HCC). Experimental studies have established that WHV causes HCC in woodchucks and woodchucks chronically infected with WHV have been used as a model to test a number of anti-viral agents. For example, the nucleoside analogue 3T3 was observed to cause dose dependent reduction in virus (50% reduction after two daily treatments at the highest dose) (Hurwitz *et al.*, 1998. *Antimicrob. Agents Chemother.*, 42, 2804-2809).

HCV Cell Culture Models

Although there have been reports of replication of HCV in cell culture (see below), these systems are difficult to replicate and have proven unreliable. Therefore, as was the case for development of other anti-HCV therapeutics such as interferon and ribavirin, after demonstration of safety in animal studies applicant can proceed directly into a clinical feasibility study.

Several recent reports have documented *in vitro* growth of HCV in human cell lines (Mizutani *et al.*, *Biochem Biophys Res Commun* 1996 227(3):822-826; Tagawa *et al.*, *Journal of Gastroenterology and Hepatology* 1995 10(5):523-527; Cribier *et al.*, *Journal of General Virology* 76(10):2485-2491; Seipp *et al.*, *Journal of General Virology* 1997 78(10):2467-2478; Iacovacci *et al.*, *Research Virology* 1997 148(2):147-151; Iacovacci *et al.*, *Hepatology* 1997 26(5) 1328-1337; Ito *et al.*, *Journal of General Virology* 1996 77(5):1043-1054; Nakajima *et al.*, *Journal of Virology* 1996 70(5):3325-3329; Mizutani *et al.*, *Journal of Virology* 1996 70(10):7219-7223; Valli *et al.*, *Res Virol* 1995 146(4): 285-288; Kato *et al.*, *Biochem Biophys Res Comm* 1995 206(3):863-869). Replication of HCV has been demonstrated in both T and B cell lines as well as cell lines derived from human hepatocytes. Demonstration of replication was documented using either RT-PCR based assays or the b-DNA assay. It is important to note that the most recent publications regarding HCV cell cultures document replication for up to 6-months.

Additionally, another recent study has identified more robust strains of hepatitis C virus having adaptive mutations that allow the strains to replicate more vigorously in human cell culture. The mutations that confer this enhanced ability to replicate are located in a specific region of a protein identified as NS5A. Studies performed at Rockefeller University have shown that in certain cell culture systems, infection with the robust strains produces a 10,000-

fold increase in the number of infected cells. The greatly increased availability of HCV-infected cells in culture can be used to develop high-throughput screening assays, in which a large number of compounds, such as enzymatic nucleic acid molecules, can be tested to determine their effectiveness.

In addition to cell lines that can be infected with HCV, several groups have reported the successful transformation of cell lines with cDNA clones of full-length or partial HCV genomes (Harada *et al.*, Journal of General Virology 1995 76(5):1215-1221; Haramatsu *et al.*, Journal of Viral Hepatitis 1997 4S(1):61-67; Dash *et al.*, American Journal of Pathology 1997 151(2):363-373; Mizuno *et al.*, Gastroenterology 1995 109(6):1933-40; Yoo *et al.*, Journal Of Virology 1995 69(1):32-38).

HCV Animal Models

The best characterized animal system for HCV infection is the chimpanzee. Moreover, the chronic hepatitis that results from HCV infection in chimpanzees and humans is very similar. Although clinically relevant, the chimpanzee model suffers from several practical impediments that make use of this model difficult. These include; high cost, long incubation requirements and lack of sufficient quantities of animals. Due to these factors, a number of groups have attempted to develop rodent models of chronic hepatitis C infection. While direct infection has not been possible several groups have reported on the stable transfection of either portions or entire HCV genomes into rodents (Yamamoto *et al.*, Hepatology 1995 22(3): 847-855; Galun *et al.*, Journal of Infectious Disease 1995 172(1):25-30; Koike *et al.*, Journal of general Virology 1995 76(12):3031-3038; Pasquinelli *et al.*, Hepatology 1997 25(3): 719-727; Hayashi *et al.*, Princess Takamatsu Symp 1995 25:1430149; Mariya K, Yotsuyanagi H, Shintani Y, Fujie H, Ishibashi K, Matsuura Y, Miyamura T, Koike K. Hepatitis C virus core protein induces hepatic steatosis in transgenic mice. Journal of General Virology 1997 78(7) 1527-1531; Takehara *et al.*, Hepatology 1995 21(3):746-751; Kawamura *et al.*, Hepatology 1997 25(4): 1014-1021). In addition, transplantation of HCV infected human liver into immunocompromised mice results in prolonged detection of HCV RNA in the animal's blood.

Vierling, International PCT Publication No. WO 99/16307, describes a method for expressing hepatitis C virus in an *in vivo* animal model. Viable, HCV infected human hepatocytes are transplanted into a liver parenchyma of a scid/scid mouse host. The scid/scid mouse host is then maintained in a viable state, whereby viable, morphologically intact human hepatocytes persist in the donor tissue and hepatitis C virus is replicated in the persisting human hepatocytes. This model provides an effective means for the study of HCV inhibition by enzymatic nucleic acids *in vivo*.

Indications

Particular degenerative and disease states that can be associated with HBV expression modulation include, but are not limited to, HBV infection, hepatitis, cancer, tumorigenesis, cirrhosis, liver failure and other conditions related to the level of HBV.

Particular degenerative and disease states that can be associated with HCV expression modulation include, but are not limited to, HCV infection, hepatitis, cancer, tumorigenesis, cirrhosis, liver failure and other conditions related to the level of HCV.

The present body of knowledge in HBV and HCV research indicates the need for methods to assay HBV or HCV activity and for compounds that can regulate HBV and HCV expression for research, diagnostic, and therapeutic use.

Lamivudine (3TC®), L-FMAU, adefovir dipivoxil, type 1 Interferon (e.g., interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon 2b, and polyethylene glycol consensus interferon), therapeutic vaccines, steroids, and 2'-5' Oligoadenylates are non-limiting examples of pharmaceutical agents that can be combined with or used in conjunction with the nucleic acid molecules (e.g. ribozymes and antisense molecules) of the instant invention. Those skilled in the art will recognize that other drugs or other therapies can similarly and readily be combined with the nucleic acid molecules of the instant invention (e.g. ribozymes and antisense molecules) and are, therefore, within the scope of the instant invention.

Diagnostic uses

The nucleic acid molecules of this invention can be used as diagnostic tools to examine genetic drift and mutations within diseased cells or to detect the presence of HBV or HCV RNA in a cell. For example, the close relationship between enzymatic nucleic acid activity and the structure of the target RNA allows the detection of mutations in any region of the molecule which alters the base-pairing and three-dimensional structure of the target RNA. By using multiple enzymatic nucleic acids described in this invention, one can map nucleotide changes which are important to RNA structure and function *in vitro*, as well as in cells and tissues. Cleavage of target RNAs with enzymatic nucleic acids can be used to inhibit gene expression and define the role (essentially) of specified gene products in the progression of disease. In this manner, other genetic targets can be defined as important mediators of the disease. These experiments can lead to better treatment of the disease progression by affording the possibility of combinational therapies (e.g., multiple enzymatic nucleic acid molecules targeted to different genes, enzymatic nucleic acid molecules coupled

with known small molecule inhibitors, or intermittent treatment with combinations of enzymatic nucleic acid molecules and/or other chemical or biological molecules). Other *in vitro* uses of enzymatic nucleic acid molecules of this invention are well known in the art, and include detection of the presence of mRNAs associated with HBV or HCV-related condition. Such RNA is detected by determining the presence of a cleavage product after treatment with an enzymatic nucleic acid using standard methodology.

In a specific example, enzymatic nucleic acid molecules which can cleave only wild-type or mutant forms of the target RNA are used for the assay. The first enzymatic nucleic acid is used to identify wild-type RNA present in the sample and the second enzymatic nucleic acid is used to identify mutant RNA in the sample. As reaction controls, synthetic substrates of both wild-type and mutant RNA can be cleaved by both enzymatic nucleic acid molecules to demonstrate the relative ribozyme efficiencies in the reactions and the absence of cleavage of the "non-targeted" RNA species. The cleavage products from the synthetic substrates can also serve to generate size markers for the analysis of wild-type and mutant RNAs in the sample population. Thus each analysis involves two enzymatic nucleic acid molecules, two substrates and one unknown sample which is combined into six reactions. The presence of cleavage products is determined using an RNase protection assay so that full-length and cleavage fragments of each RNA can be analyzed in one lane of a polyacrylamide gel. It is not absolutely required to quantify the results to gain insight into the expression of mutant RNAs and putative risk of the desired phenotypic changes in target cells. The expression of mRNA whose protein product is implicated in the development of the phenotype (*i.e.*, HBV or HCV) is adequate to establish risk. If probes of comparable specific activity are used for both transcripts, then a qualitative comparison of RNA levels is adequate and will decrease the cost of the initial diagnosis. Higher mutant form to wild-type ratios are correlated with higher risk whether RNA levels are compared qualitatively or quantitatively.

Additional Uses

Potential usefulness of sequence-specific enzymatic nucleic acid molecules of the instant invention have many of the same applications for the study of RNA that DNA restriction endonucleases have for the study of DNA (Nathans *et al.*, 1975 *Ann. Rev. Biochem.* 44:273). For example, the pattern of restriction fragments can be used to establish sequence relationships between two related RNAs, and large RNAs can be specifically cleaved to fragments of a size more useful for study. The ability to engineer sequence specificity of the enzymatic nucleic acid molecule is ideal for cleavage of RNAs of unknown sequence. Applicant describes the use of nucleic acid molecules to down-regulate gene

expression of target genes in bacterial, microbial, fungal, viral, and eukaryotic systems including plant, or mammalian cells.

All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the invention pertains. All references cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually.

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art, which are encompassed within the spirit of the invention, are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. Thus, such additional embodiments are within the scope of the present invention and the following claims.

The invention illustratively described herein suitably can be practiced in the absence of any element or elements, limitation or limitations that are not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments, optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the description and the appended claims.

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

TABLE I

Characteristics of naturally occurring ribozymes

Group I Introns

- Size: ~150 to >1000 nucleotides.
- Requires a U in the target sequence immediately 5' of the cleavage site.
- Binds 4-6 nucleotides at the 5'-side of the cleavage site.
- Reaction mechanism: attack by the 3'-OH of guanosine to generate cleavage products with 3'-OH and 5'-guanosine.
- Additional protein cofactors required in some cases to help folding and maintenance of the active structure.
- Over 300 known members of this class. Found as an intervening sequence in *Tetrahymena thermophila* rRNA, fungal mitochondria, chloroplasts, phage T4, blue-green algae, and others.
- Major structural features largely established through phylogenetic comparisons, mutagenesis, and biochemical studies [i,ii].
- Complete kinetic framework established for one ribozyme [iii,iv,v,vi].
- Studies of ribozyme folding and substrate docking underway [vii,viii,ix].
- Chemical modification investigation of important residues well established [x,xi].
- The small (4-6 nt) binding site may make this ribozyme too non-specific for targeted RNA cleavage, however, the *Tetrahymena* group I intron has been used to repair a "defective" β -galactosidase message by the ligation of new β -galactosidase sequences onto the defective message [xii].

RNase P RNA (M1 RNA)

- Size: ~290 to 400 nucleotides.
- RNA portion of a ubiquitous ribonucleoprotein enzyme.

- Cleaves tRNA precursors to form mature tRNA [xiii].
- Reaction mechanism: possible attack by M^{2+} -OH to generate cleavage products with 3'-OH and 5'-phosphate.
- RNase P is found throughout the prokaryotes and eukaryotes. The RNA subunit has been sequenced from bacteria, yeast, rodents, and primates.
- Recruitment of endogenous RNase P for therapeutic applications is possible through hybridization of an External Guide Sequence (EGS) to the target RNA [xiv,xv]
- Important phosphate and 2' OH contacts recently identified [xvi,xvii]

Group II Introns

- Size: >1000 nucleotides.
- Trans cleavage of target RNAs recently demonstrated [xviii,xix].
- Sequence requirements not fully determined.
- Reaction mechanism: 2'-OH of an internal adenosine generates cleavage products with 3'-OH and a "lariat" RNA containing a 3'-5' and a 2'-5' branch point.
- Only natural ribozyme with demonstrated participation in DNA cleavage [xx,xxi] in addition to RNA cleavage and ligation.
- Major structural features largely established through phylogenetic comparisons [xxii].
- Important 2' OH contacts beginning to be identified [xxiii]
- Kinetic framework under development [xxiv]

Neurospora VS RNA

- Size: ~144 nucleotides.
- Trans cleavage of hairpin target RNAs recently demonstrated [xxv].

- Sequence requirements not fully determined.
- Reaction mechanism: attack by 2'-OH 5' to the scissile bond to generate cleavage products with 2',3'-cyclic phosphate and 5'-OH ends.
- Binding sites and structural requirements not fully determined.
- Only 1 known member of this class. Found in *Neurospora* VS RNA.

Hammerhead Ribozyme

(see text for references)

- Size: ~13 to 40 nucleotides.
- Requires the target sequence UH immediately 5' of the cleavage site.
- Binds a variable number nucleotides on both sides of the cleavage site.
- Reaction mechanism: attack by 2'-OH 5' to the scissile bond to generate cleavage products with 2',3'-cyclic phosphate and 5'-OH ends.
- 14 known members of this class. Found in a number of plant pathogens (virusoids) that use RNA as the infectious agent.
- Essential structural features largely defined, including 2 crystal structures [xxvi,xxvii]
- Minimal ligation activity demonstrated (for engineering through *in vitro* selection) [xxviii]
- Complete kinetic framework established for two or more ribozymes [xxix].
- Chemical modification investigation of important residues well established [xxx].

Hairpin Ribozyme

- Size: ~50 nucleotides.
- Requires the target sequence GUC immediately 3' of the cleavage site.

- Binds 4-6 nucleotides at the 5'-side of the cleavage site and a variable number to the 3'-side of the cleavage site.
- Reaction mechanism: attack by 2'-OH 5' to the scissile bond to generate cleavage products with 2',3'-cyclic phosphate and 5'-OH ends.
- 3 known members of this class. Found in three plant pathogen (satellite RNAs of the tobacco ringspot virus, arabis mosaic virus and chicory yellow mottle virus) which uses RNA as the infectious agent.
- Essential structural features largely defined [xxxix, xl, xlii, xliii, xliv]
- Ligation activity (in addition to cleavage activity) makes ribozyme amenable to engineering through *in vitro* selection [xlv]
- Complete kinetic framework established for one ribozyme [xlvi]
- Chemical modification investigation of important residues begun [xlvii, xlviii]

Hepatitis Delta Virus (HDV) Ribozyme

- Size: ~60 nucleotides.
- Trans cleavage of target RNAs demonstrated [xlix].
- Binding sites and structural requirements not fully determined, although no sequences 5' of cleavage site are required. Folded ribozyme contains a pseudoknot structure [xl].
- Reaction mechanism: attack by 2'-OH 5' to the scissile bond to generate cleavage products with 2',3'-cyclic phosphate and 5'-OH ends.
- Only 2 known members of this class. Found in human HDV.
- ^{xi}Circular form of HDV is active and shows increased nuclease stability [xlii]

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Table II:**A. 2.5 μ mol Synthesis Cycle ABI 394 Instrument**

Reagent	Equivalents	Amount	Wait Time* DNA	Wait Time* 2'-O-methyl	Wait Time*RNA
Phosphoramidites	6.5	163 μ L	45 sec	2.5 min	7.5 min
S-Ethyl Tetrazole	23.8	238 μ L	45 sec	2.5 min	7.5 min
Acetic Anhydride	100	233 μ L	5 sec	5 sec	5 sec
N-Methyl Imidazole	186	233 μ L	5 sec	5 sec	5 sec
TCA	176	2.3 mL	21 sec	21 sec	21 sec
Iodine	11.2	1.7 mL	45 sec	45 sec	45 sec
Beaucage	12.9	645 μ L	100 sec	300 sec	300 sec
Acetonitrile	NA	6.67 mL	NA	NA	NA

B. 0.2 μ mol Synthesis Cycle ABI 394 Instrument

Reagent	Equivalents	Amount	Wait Time* DNA	Wait Time* 2'-O-methyl	Wait Time*RNA
Phosphoramidites	15	31 μ L	45 sec	233 sec	465 sec
S-Ethyl Tetrazole	38.7	31 μ L	45 sec	233 min	465 sec
Acetic Anhydride	655	124 μ L	5 sec	5 sec	5 sec
N-Methyl Imidazole	1245	124 μ L	5 sec	5 sec	5 sec
TCA	700	732 μ L	10 sec	10 sec	10 sec
Iodine	20.6	244 μ L	15 sec	15 sec	15 sec
Beaucage	7.7	232 μ L	100 sec	300 sec	300 sec
Acetonitrile	NA	2.64 mL	NA	NA	NA

C. 0.2 μ mol Synthesis Cycle 96 well Instrument

Reagent	Equivalents:DNA/ 2'-O-methyl/Ribo	Amount: DNA/2'-O- methyl/Ribo	Wait Time* DNA	Wait Time* 2'-O- methyl	Wait Time* Ribo
Phosphoramidites	22/33/66	40/60/120 μ L	60 sec	180 sec	360sec
S-Ethyl Tetrazole	70/105/210	40/60/120 μ L	60 sec	180 min	360 sec
Acetic Anhydride	265/265/265	50/50/50 μ L	10 sec	10 sec	10 sec
N-Methyl Imidazole	502/502/502	50/50/50 μ L	10 sec	10 sec	10 sec
TCA	238/475/475	250/500/500 μ L	15 sec	15 sec	15 sec
Iodine	6.8/6.8/6.8	80/80/80 μ L	30 sec	30 sec	30 sec
Beaucage	34/51/51	80/120/120	100 sec	200 sec	200 sec
Acetonitrile	NA	1150/1150/1150 μ L	NA	NA	NA

- Wait time does not include contact time during delivery.

Table III: HBV Strains and Accession numbers

Accession Number	NAME
AF100308.1	AF100308 Hepatitis B virus strain 2-18, complete
AB026815.1	AB026815 Hepatitis B virus DNA, complete genome,
AB033559.1	AB033559 Hepatitis B virus DNA, complete genome,
AB033558.1	AB033558 Hepatitis B virus DNA, complete genome,
AB033557.1	AB033557 Hepatitis B virus DNA, complete genome,
AB033556.1	AB033556 Hepatitis B virus DNA, complete genome,
AB033555.1	AB033555 Hepatitis B virus DNA, complete genome,
AB033554.1	AB033554 Hepatitis B virus DNA, complete genome,
AB033553.1	AB033553 Hepatitis B virus DNA, complete genome,
AB033552.1	AB033552 Hepatitis B virus DNA, complete genome,
AB033551.1	AB033551 Hepatitis B virus DNA, complete genome,
AB033550.1	AB033550 Hepatitis B virus DNA, complete genome
AF143308.1	AF143308 Hepatitis B virus clone WB1254, complete
AF143307.1	AF143307 Hepatitis B virus clone RM518, complete
AF143306.1	AF143306 Hepatitis B virus clone RM517, complete
AF143305.1	AF143305 Hepatitis B virus clone RM501, complete
AF143304.1	AF143304 Hepatitis B virus clone HD319, complete
AF143303.1	AF143303 Hepatitis B virus clone HD1406, complete
AF143302.1	AF143302 Hepatitis B virus clone HD1402, complete
AF143301.1	AF143301 Hepatitis B virus clone BW1903, complete
AF143300.1	AF143300 Hepatitis B virus clone 7832-G4, complete
AF143299.1	AF143299 Hepatitis B virus clone 7744-G9, complete
AF143298.1	AF143298 Hepatitis B virus clone 7720-G8, complete
AB026814.1	AB026814 Hepatitis B virus DNA, complete genome,
AB026813.1	AB026813 Hepatitis B virus DNA, complete genome,
AB026812.1	AB026812 Hepatitis B virus DNA, complete genome,
AB026811.1	AB026811 Hepatitis B virus DNA, complete genome,
AJ131956.1	HBV131956 Hepatitis B virus complete genome,
AF151735.1	AF151735 Hepatitis B virus, complete genome
AF090842.1	AF090842 Hepatitis B virus strain G5.27295, complete
AF090841.1	AF090841 Hepatitis B virus strain G4.27241, complete
AF090840.1	AF090840 Hepatitis B virus strain G3.27270, complete
AF090839.1	AF090839 Hepatitis B virus strain G2.27246, complete
AF090838.1	AF090838 Hepatitis B virus strain P1.27239, complete
Y18858.1	HBV18858 Hepatitis B virus complete genome, isolate
Y18857.1	HBV18857 Hepatitis B virus complete genome, isolate
D12980.1	HPBCG Hepatitis B virus subtype adr(SRADR) DNA,
Y18856.1	HBV18856 Hepatitis B virus complete genome, isolate
Y18855.1	HBV18855 Hepatitis B virus complete genome, isolate
AJ131133.1	HBV131133 Hepatitis B virus, complete genome, strain
X80925.1	HBVP6PCXX Hepatitis B virus (patient 6) complete
X80926.1	HBVP5PCXX Hepatitis B virus (patient 5) complete
X80924.1	HBVP4PCXX Hepatitis B virus (patient 4) complete

AF100309.1	Hepatitis B virus strain 56, complete genome
AF068756.1	AF068756 Hepatitis B virus, complete genome
AF043593.1	AF043593 Hepatitis B virus isolate 6/89, complete
Y07587.1	HBVAYWGEN Hepatitis B virus, complete genome
D28880.1	D28880 Hepatitis B virus DNA, complete genome, strain
X98076.1	HBVDEFVP3 Hepatitis B virus complete genome with
X98075.1	HBVDEFVP2 Hepatitis B virus complete genome with
X98074.1	HBVDEFVP1 Hepatitis B virus complete genome with
X98077.1	HBVCGWITY Hepatitis B virus complete genome, wild type
X98072.1	HBVCGINSC Hepatitis B virus complete genome with
X98073.1	HBVCGINCX Hepatitis B virus complete genome with
U95551.1	U95551 Hepatitis B virus subtype ayw, complete genome
D23684.1	HPBC6T588 Hepatitis B virus (C6-TKB588) complete genome
D23683.1	HPBC5HKO2 Hepatitis B virus (C5-HBVKO2) complete genome
D23682.1	HPBB5HKO1 Hepatitis B virus (B5-HBVKO1) complete genome
D23681.1	HPBC4HST2 Hepatitis B virus (C4-HBVST2) complete genome
D23680.1	HPBB4HST1 Hepatitis B virus (B4-HBVST1) complete genome
D00331.1	HPBADW3 Hepatitis B virus genome, complete genome
D00330.1	HPBADW2 Hepatitis B virus genome, complete genome
D50489.1	HPBA11A Hepatitis B virus DNA, complete genome
D23679.1	HPBA3HMS2 Hepatitis B virus (A3-HBVMS2) complete genome
D23678.1	HPBA2HYS2 Hepatitis B virus (A2-HBVYS2) complete genome
D23677.1	HPBA1HKK2 Hepatitis B virus (A1-HBVKK2) complete genome
D16665.1	HPBADRM Hepatitis B virus DNA, complete genome
D00329.1	HPBADW1 Hepatitis B virus (HBV) genome, complete genome
X97851.1	HBVP6CSX Hepatitis B virus (patient 6) complete genome
X97850.1	HBVP4CSX Hepatitis B virus (patient 4) complete genome
X97849.1	HBVP3CSX Hepatitis B virus (patient 3) complete genome
X97848.1	HBVP2CSX Hepatitis B virus (patient 2) complete genome
X51970.1	HVHEPB Hepatitis B virus (HBV 991) complete genome
M38636.1	HPBCGADR Hepatitis B virus, subtype adr, complete genome
X59795.1	HBVAYWMCG Hepatitis B virus (ayw subtype mutant)
M38454.1	HPBADR1CG Hepatitis B virus , complete genome
M32138.1	HPBHBVAA Hepatitis B virus variant HBV-alpha1, complete
J02203.1	HPBAYW Human hepatitis B virus (subtype ayw), complete
M12906.1	HPBADRA Hepatitis B virus subtype adr, complete genome
M54923.1	HPBADWZ Hepatitis B virus (subtype adw), complete genome
L27106.1	HPBMUT Hepatitis B virus mutant complete genome

Table IV: HBV Substrate Sequence

NT Position*	SUBSTRATE	SEQ ID
82	CUAUCGUGCCCUUCUUCAUC	1.
101	CUACCGUCCGGCC	2.
159	CUUCUCAUCU	3.
184	CUUCCCUUACCAC	4.
269	GACUCUCAGAAUGUCAACGAC	5.
381	CUGUAGGCAUAAUUGGUCUG	6.
401	GUUCACCAGCACCAUGCAACUUUUU	7.
424	UUUCACGUCUGCCUAAUCAUC	8.
524	AUUUGGAGCUUC	9.
562	CUGACUUCUJUCCUUCUAUUC	10.
649	CUCACCAUACCGCACUCA	11.
667	GGCAAGCUAUUCUGUG	12.
717	GGAAGUAAUUGGAAGAC	13.
758	CAGCUAUGUCAUGUUA	14.
783	CUAAAUCGGCCUAAAUCAGAC	15.
812	CAUUUCCUGUCUCACUUUUGGAAGAG	16.
887	UCCUGCUUACAGAC	17.
922	CAACACUUCGGAAACUACUGUUGUAG	18.
989	CUCGCCUCGCAGACGAAGGUCUC	19.
1009	CAAUCGCCGCGUCGCAGAAG	20.
1031	AUCUCAUUCUCGGGAUCUCAA	21.
1052	AUGUUAGUAUCCCUUGGACUC	22.
1072	CAUAAGGUGGGAAACUUUACUG	23.
1109	CUGUACCUAUUCUUUAAAUCC	24.
1127	CUGAGUGGCAACUCCC	25.
1271	CCAAUAUUCUGCCCUUGGACAA	26.
1297	AUUAACCAUAUUAUCCUGAACA	27.
1319	AUGCAGUAAUCAUUACUCAAACUA	28.
1340	AAACUAGGCAUUA	29.
1370	AGGCGGGCAUUCUAUUAAGAGAG	30.
1393	GAAACUACGCGCAGCGCCUCAUUUUGU	31.
1412	CAUUUUGUGGGUCACCAUA	32.
1441	CAAGAGCUACAGCAUGGG	33.

LOCUS HPBADR1CG 3221 bp DNA circular VRL
06-MAR-1995
DEFINITION Hepatitis B virus , complete genome.
ACCESSION M38454

*The nucleotide number referred to in that table is the position of the 5' end of the oligo in this sequence.

TABLE V: HUMAN HBV HAMMERHEAD RIBOZYME AND TARGET SEQUENCE

Pos	Substrate	Seq ID	Hammerhead	Seq ID
13	CCACCACU U UCCACCAA	34	UUGGUGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUGGUGG	7434
14	CACCACUU U CCACCAA	35	UUUGGUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGUGGUG	7435
15	ACCACUUU C CACCAAAC	36	GUUUGGUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAAGUGGU	7436
25	ACCAACU C UUCAAGAU	37	AUCUUGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUUUGGU	7437
27	CAAAUCU U CAAGAUC	38	GGAUUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAGUUUG	7438
28	AAACUCU C AAGAUC	39	GGGAUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGAGUUU	7439
34	UUCAAGAU C CCAGAGUC	40	GACUCUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUCUUGAA	7440
42	CCCAGAGU C AGGGCCCU	41	AGGGCCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACUCUGGG	7441
53	GGCCUGU A CUUCCUG	42	CAGGAAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACAGGGCC	7442
56	CCUGUACU U UCCUGCUG	43	CAGCAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUACAGG	7443
57	CUGUACUU U CCUGCUGG	44	CCAGCAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGUACAG	7444
58	UGUACUUU C CUGCUGGU	45	ACCAGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAAGUACA	7445
71	UGGUGGCU C CAGUUCAG	46	CUGAACUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGCCACCA	7446
76	GCUCAGU U CAGGAACA	47	UGUCCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACUGGAGC	7447
77	CUCAGUU C AGGAACAG	48	CUGUCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AACUGGAG	7448
97	GCCUGCU C AGAAUACU	49	AGUAUUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGCAGGGC	7449
103	CUCAGAAU A CUGUCUCU	50	AGAGACAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUUCUGAG	7450
108	AAUACUGU C UCUGCCAU	51	AUGGCAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACAGUAUU	7451
110	UACUGUCU C UGCCAUU	52	AUAUGGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGACGUA	7452
117	UCUGCCAU A UCGUCAAU	53	AUUGACGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUGGCAGA	7453
119	UGCCAUU C GUCAAUCU	54	AGAUUGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUAUGGCA	7454
122	CAUAUCGU C AAUCUUAU	55	AUAAGAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACGAUUUG	7455
126	UCGUCAAU C UUAUCGAA	56	UUCGAUAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUUGACGA	7456
128	GUCAAUCU U AUCGAAGA	57	UCUUCGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAUUGAC	7457
129	UCAAUUCU A UCGAAGAC	58	GUCUUCGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGAUUGA	7458
131	AAUCUUAU C GAAGACUG	59	CAGUCUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUAAGAUU	7459
150	GACCCUGU A CCGAACAU	60	AUGUUCGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACAGGGUC	7460
168	GAGAACAU C GCAUCAGG	61	CCUGAUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUGUUCUC	7461
173	CAUCGCAU C AGGACUCC	62	GGAGUCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUGCAGUG	7462
180	UCAGGACU C CUAGGACC	63	GGUCCUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUCCUGA	7463
183	GGACUCCU A GGACCCCU	64	AGGGGUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGAGUCC	7464
195	CCCUGCU C GUGUACA	65	UGUAACAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGCAGGGG	7465
200	GCUCGUGU U ACAGGCGG	66	CCGCCUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACACGAGC	7466
201	CUCGUGUU A CAGGCGGG	67	CCCGCCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AACACGAG	7467
212	GGCGGGGU U UUUUUUGU	68	ACAAGAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACCCCGCC	7468
213	GCGGGGUU U UUCUUGUU	69	AACAAGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AACCCCGC	7469
214	CGGGGUUU U UCUUGUUG	70	CAACAAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAACCCCG	7470
215	GGGGUUUU U CUUGUUGA	71	UCAACAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAAACCCC	7471
216	GGGUUUUU C UUGUUGAC	72	GUCAACAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAAAACC	7472
218	GUUUUUUU U GUUGACAA	73	UUGUCAAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAAAAAC	7473
221	UUUCUUGU U GACAAAAA	74	UUUUUGUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACAAGAAA	7474
231	ACAAAAAU C CUCACAAU	75	AUUGUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUUUUUUG	7475
234	AAAAUCCU C ACAAUACC	76	GGUAUUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGAUUUU	7476
240	CUCACAAU A CCACAGAG	77	CUCUGUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUUGUGAG	7477
250	CACAGAGU C UAGACUCG	78	CGAGUCUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACUCUGUG	7478
252	CAGAGUCU A GACUCGUG	79	CACGAGUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGACUCUG	7479

257	UCUAGACU C GUGGUGGA	80	UCCACCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCUAGA	7480
268	GGUGGACU U CUCUCAAU	81	AUUGAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCACC	7481
269	GUGGACUU C UCACAAUU	82	AAUUGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUCCAC	7482
271	GGACUUCU C UCAAUUUU	83	AAAAUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGUCC	7483
273	ACUUCUCU C AAUUUUCU	84	AGAAAAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGAAGU	7484
277	CUCUCAAU U UUCUAGGG	85	CCCUAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGAGAG	7485
278	UCUCAAUU U UCUGAGGG	86	CCCCUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGAGA	7486
279	CUCAAUUU U CUAGGGGG	87	CCCCCUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUUGAG	7487
280	UCAAUUUU C UAGGGGGA	88	UCCCCCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAUUGA	7488
282	AAUUUUCU A GGGGGAAC	89	GUUCCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAAAUU	7489
301	CCGUGUGU C UUGGCCAA	90	UUGGCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACACGG	7490
303	GUGUGUCU U GGCCAAAA	91	UUUUGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACACAC	7491
313	GCCAAAAU U CGCAGUCC	92	GGACUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUGGC	7492
314	CCAAAAUU C GCAGUCCC	93	GGGACUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUUUGG	7493
320	UUCGCAGU C CCAAUUCU	94	AGAUUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGCGAA	7494
327	UCCCAAAU C UCCAGUCA	95	UGACUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUGGGA	7495
329	CCAAAUUC C CAGUCACU	96	AGUGACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUUGG	7496
334	UCUCCAGU C ACUCACCA	97	UGGUGAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGGAGA	7497
338	CAGUCACU C ACCAACCU	98	AGGUUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGACUG	7498
349	CAACCUGU U GUCCUCCA	99	UGGAGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGGUUG	7499
352	CCUGUUGU C CUCCAUUU	100	AAUUGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAACAGG	7500
355	GUUGUCCU C CAAUUUGU	101	ACAAAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGACAAC	7501
360	CCUCCA AU U UGUCCUGG	102	CCAGGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGGAGG	7502
361	CUCCA AUU U GUCCUGGU	103	ACCAGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGGAG	7503
364	CAAUUUGU C CUGGUUAU	104	AUAACCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAUUG	7504
370	GUCCUGGU U AUCGUGG	105	CCAGCGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAGGAC	7505
371	UCCUGGUU A UCGCUGGA	106	UCCAGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCAGGA	7506
373	CUGGUUAU C GCUGGAUG	107	CAUCCAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAACCAG	7507
385	GGAUGUGU C UGCGGCGU	108	ACGCCGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACAUCC	7508
394	UGCGGCGU U UUAUCAUC	109	GAUGAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGCCGCA	7509
395	GCGGCGUU U UAUCAUCU	110	AGAUGAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACGCCGC	7510
396	CGGCGUUU U AUCAUCUU	111	AAGAUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACGCCG	7511
397	GGCGUUUU A UCAUCUUC	112	GAAGAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAACGCC	7512
399	CGUUUUAU C AUCUCCU	113	AGGAAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAAACG	7513
402	UUUAUCAU C UUCCUCUG	114	CAGAGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUAAA	7514
404	UAUCAUCU U CCUCUGCA	115	UGCAGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGAUA	7515
405	AUCAUCUU C CUCUGCAU	116	AUGCAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUGAU	7516
408	AUCUCCU C UGCAUCCU	117	AGGAUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAAGAU	7517
414	CUCUGCAU C CUGCUGCU	118	AGCAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAGAG	7518
423	CUGCUGCU A UGCCUCAU	119	AUGAGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGCAG	7519
429	CUAUGCCU C AUCUUCUU	120	AAGAAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAUAG	7520
432	UGCCUCAU C UUCUUGUU	121	AACAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAGGCA	7521
434	CCUCAUCU U CUUGUUGG	122	CCAACAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGAGG	7522
435	CUCAUCUU C UUGUUGGU	123	ACCAACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUGAG	7523
437	CAUCUUCU U GUUGGUUC	124	GAACCAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGAU	7524
440	CUUCUUGU U GGUUCUUC	125	GAAGAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAGAA	7525
444	UUGUUGGU U CUUCUGGA	126	UCCAGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAACAA	7526
445	UGUUGGUU C UUCUGGAC	127	GUCCAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCAACA	7527
447	UUGGUUCU U CUGGACUA	128	UAGUCCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAACCAA	7528
448	UGGUUCUU C UGGACUAU	129	AUAGUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAACCA	7529
455	UCUGGACU A UCAAGGUA	130	UACCUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCAGA	7530

457	UGGACUUAU C AAGGUAUG	131	CAUACCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGUCCA	7531
463	AUCAAGGU A UGUUGCCC	132	GGGCAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUUGAU	7532
467	AGGUAUGU U GCCCGUUU	133	AAACGGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUACCU	7533
474	UUGCCCGU U UGUCCUCU	134	AGAGGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGCAA	7534
475	UGCCCGUU U GUCCUCUA	135	UAGAGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACGGGCA	7535
478	CCGUUUGU C CUCUAAUU	136	AAUUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAACGG	7536
481	UUUGUCCU C UAAUUGCA	137	UGGAAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGACAAA	7537
483	UGUCCUCU A AUUCCAGG	138	CCUGGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGGACA	7538
486	CCUCUAAU U CCAGGAUC	139	GAUCCUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAGAGG	7539
487	CUCUAAUU C CAGGAUCA	140	UGAUCCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGAGG	7540
494	UCCAGGAU C AUCAACAA	141	UUGUUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCUGGA	7541
497	AGGAUCAU C AACAAACA	142	UGGUUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUCCU	7542
535	GCACAACU C CUGCUCAA	143	UUGAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGUGC	7543
541	CUCCUGCU C AAGGAACC	144	GGUUCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGGAG	7544
551	AGGAACCU C UAUGUUUC	145	GAAACUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUCCU	7545
553	GAACCUCU A UGUUUGCC	146	GGGAAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGGUUC	7546
557	CUCUAUGU U UCCUCUAA	147	AUGAGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUAGAG	7547
558	UCUAUGUU U CCCUCAUG	148	CAUGAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUAGA	7548
559	CUAUGUUU C CCUCAUGU	149	ACAUGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACUAGG	7549
563	GUUUGCCU C AUGUUGCU	150	AGCAACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGAAAC	7550
568	CCUCAUGU U GCUGUACA	151	UGUACAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUGAGG	7551
574	GUUGCUGU A CAAAACCU	152	AGGUUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGCAAC	7552
583	CAAAACCU A CGGACGGA	153	UCCGUCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUUUG	7553
604	GCACCUGU A UUCCCAUC	154	GAUGGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGGUGC	7554
606	ACCUGUAU U CCCAUCCC	155	GGGAUGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACAGGU	7555
607	CCUGUAUU C CCAUCCCA	156	UGGGAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUACAGG	7556
612	AUUCCTAU C CCAUCAUC	157	GAUGAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGGAAU	7557
617	CAUCCCAU C AUCUUGGG	158	CCCAAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGGAUG	7558
620	CCCAUCAU C UUGGGCUU	159	AAGCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUGGG	7559
622	CAUCAUCU U GGGCUUUC	160	GAAAGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGAUG	7560
628	CUUGGGCU U UCGCAAAA	161	UUUUGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCAAG	7561
629	UUGGGCUU U CGCAAAAU	162	AUUUUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCCAA	7562
630	UGGGCUUU C GCAAAUAU	163	UAUUUUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCCA	7563
638	CGCAAAAU A CCUAUGGG	164	CCCAUAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUGCG	7564
642	AAAUACCU A UGGGAGUG	165	CACUCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUUUU	7565
656	GUGGGCCU C AGUCCGUU	166	AACGGACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCCAC	7566
660	GCCUCAGU C CGUUUCUC	167	GAGAAACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAGGC	7567
664	CAGUCCGU U UCUCUUGG	168	CCAAGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGACUG	7568
665	AGUCCGUU U CUCUUGGC	169	GCCAAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACGGACU	7569
666	GUCCGUUU C UCUGGCUU	170	AGCCAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACGGAC	7570
668	CCGUUUUC C UUGGCUCA	171	UGAGCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAACGG	7571
670	GUUUCUCU U GGCUCAGU	172	ACUGAGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGAAAC	7572
675	UCUUGGCU C AGUUUACU	173	AGUAAACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCAAGA	7573
679	GGCUCAGU U UACUAGUG	174	CACUAGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAGCC	7574
680	GCUCAGUU U ACUAGUGC	175	GCACUAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACUGAGC	7575
681	CUCAGUUU A CUAGUGCC	176	GGCACUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACUGAG	7576
684	AGUUUACU A GUGCCAUU	177	AAUGGCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAACU	7577
692	AGUGCCAU U UGUUCAGU	178	ACUGAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGCACU	7578
693	GUGCCAUU U GUUCAGUG	179	CACUGAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGGCAC	7579
696	CCAUUUGU U CAGUGGUU	180	AACCACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAAUGG	7580
697	CAUUUGUU C AGUGGUUC	181	GAACCACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAAUUG	7581

704	UCAGUGGU U CGUAGGGC	182	GCCCUACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCACUGA	7582
705	CAGUGGUU C GUAGGGCU	183	AGCCCUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCACUG	7583
708	UGGUUCGU A GGGCUUUC	184	GAAAGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGAACCA	7584
714	GUAGGGCU U UCCCCAC	185	GUGGGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCUAC	7585
715	UAGGGCUU U CCCCCACU	186	AGUGGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCCUA	7586
716	AGGGCUUU C CCCCACUG	187	CAGUGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCCU	7587
726	CCCACUGU C UGGCUUUC	188	GAAAGCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUGGG	7588
732	GUCUGGCU U UCAGUUAU	189	AUAACUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCAGAC	7589
733	UCUGGCUU U CAGUUAUA	190	UAUAACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCAGA	7590
734	CUGGCUUU C AGUUAUAU	191	AUAUAACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCAG	7591
738	CUUUCAGU U AUAUGGAU	192	AUCCAUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAAAG	7592
739	UUUCAGUU A UAUGGAUG	193	CAUCCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACUGAAA	7593
741	UCAGUUUA A UGGAUGAU	194	AUCAUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAACUGA	7594
755	GAUGUGGU U UUGGGGGC	195	GCCCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCACAUC	7595
756	AUGUGGUU U UGGGGGCC	196	GGCCCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCACAU	7596
757	UGUGGUUU U GGGGGCCA	197	UGGCCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACCACA	7597
769	GGCCAAGU C UGUACAAC	198	GUUGUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUUGGCC	7598
773	AAGUCUGU A CAACAUCU	199	AGAUGUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGACUU	7599
780	UACAACAU C UUGAGUCC	200	GGACUCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUUGUA	7600
782	CAACAUCU U GAGUCCCU	201	AGGGACUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGUUG	7601
787	UCUUGAGU C CCUUUAUG	202	CAUAAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCAAGA	7602
791	GAGUCCCU U UAUGCCGC	203	GCGGCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGACUC	7603
792	AGUCCCUU U AUGCCGCU	204	AGCGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGACU	7604
793	GUCCCUUU A UGCCGUG	205	CAGCGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGGAC	7605
803	GCCGUGU U ACCAAUUU	206	AAAUUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGCGGC	7606
804	CCGUGUU A CCAAUUUU	207	AAAAUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAGCGG	7607
810	UUACCAAU U UUCUUUUG	208	CAAAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGGUAA	7608
811	UACCAAUU U UCUUUUGU	209	ACAAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGGUA	7609
812	ACCAAUUU U CUUUUGUC	210	GACAAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUUGGU	7610
813	CCAAUUUU C UUUUGUCU	211	AGACAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAUUGG	7611
815	AAUUUUCU U UUGUCUUU	212	AAAGACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAAAUU	7612
816	AUUUUCUU U UGUCUUUG	213	CAAAGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAAAU	7613
817	UUUUCUUU U GUCUUUGG	214	CCAAAGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAAAA	7614
820	UCUUUUGU C UUUGGGUA	215	UACCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAAAAGA	7615
822	UUUUGUCU U UGGGUUAU	216	UAUACCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACAAAA	7616
823	UUUGUCUU U GGGUAUAC	217	GUUACCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACAAA	7617
828	CUUUGGGU A UACAUUUA	218	UAAAUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCAAAG	7618
830	UUGGGUUA A CAUUUAAA	219	UUUAAAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACCCAA	7619
834	GUUACAUU U UAAACCCU	220	AGGGUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUAUAC	7620
835	UAUACAUU U AAACCCUC	221	GAGGGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGUAUA	7621
836	AUACAUUU A AACCUCUA	222	UGAGGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUGUAU	7622
843	UAAACCCU C ACAAACA	223	UGUUUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGUUUA	7623
865	AUGGGGAU A UUCCCUUA	224	UAAGGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCAU	7624
867	GGGGAUUA U CCUUAAC	225	GUUAAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUCCCC	7625
868	GGGAUUAU C CCUUAACU	226	AGUUAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUCCC	7626
872	UAUCCCCU U AACUUCAU	227	AUGAAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGAAUA	7627
873	AUUCCCUU A ACUUCAUG	228	CAUGAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGAAU	7628
877	CCUUAACU U CAUGGGAU	229	AUCCCAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUAAGG	7629
878	CUUAACUU C AUGGGUAU	230	UAUCCCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUAAG	7630
886	CAUGGGAU A UGUAAUUG	231	CAAUUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCAUG	7631
890	GGAUAUGU A AUUGGGAG	232	CUCCCAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUAUCC	7632

893	UAUGUAAU U GGGAGUUG	233	CAACUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUACAU	7633
900	UUGGGAGU U GGGGCACA	234	UGUGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCCCAA	7634
910	GGGCACAU U GCCACAGG	235	CCUGUGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUGCCC	7635
924	AGGAACAU A UUGUACAA	236	UUGUACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCCU	7636
926	GAACAUU U GUACAAA	237	UUUUGUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUGUUC	7637
929	CAUAUUGU A CAAAAAU	238	AUUUUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUAUG	7638
938	CAAAAAU C AAAAUGUG	239	CACAUUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUUUG	7639
948	AAUUGUGU U UUAGGAAA	240	UUUCCUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACAUUU	7640
949	AAUGUGUU U UAGGAAAC	241	GUUCCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACAUU	7641
950	AUGUGUUU U AGGAAACU	242	AGUUUCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACACAU	7642
951	UGUGUUUU A GGAAACUU	243	AAGUUUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAACACA	7643
959	AGGAAACU U CCUGUAAA	244	UUUACAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUCCU	7644
960	GGAAACUU C CUGUAAAC	245	GUUACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUUCC	7645
965	CUUCCUGU A AACAGGCC	246	GGCCUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGGAAG	7646
975	ACAGGCCU A UUGAUUGG	247	CCAAUCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCUGU	7647
977	AGGCCUAU U GAUUGGAA	248	UUCCAAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGGCCU	7648
981	CUAUUGAU U GGAAAGUA	249	UACUUUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCAAUAG	7649
989	UGGAAAGU A UGUCAACG	250	CGUUGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUUUCCA	7650
993	AAGUAUGU C AACGAAU	251	AAUUCGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUACUU	7651
1001	CAACGAAU U GUGGGUCU	252	AGACCCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCGUUG	7652
1008	UUGUGGGU C UUUUGGGG	253	CCCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCACA	7653
1010	GUGGGUCU U UUGGGGU	254	AACCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCCAC	7654
1011	UGGGUCUU U UGGGGUU	255	AAACCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACCCA	7655
1012	GGGUCUUU U GGGGUUG	256	CAAAACCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGACCC	7656
1018	UUUGGGGU U UGCCGCC	257	GGGCGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCCAAA	7657
1019	UUGGGGUU U GCCGCC	258	GGGCGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCCTAA	7658
1029	CCGCCCUU U UCACGCAA	259	UUGCGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGCGG	7659
1030	CGCCCCUU U CACGCAU	260	AUUGCGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGGCG	7660
1031	GCCCCUUU C ACGCAU	261	CAUUGCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGGGC	7661
1045	AUGUGGAU A UUCUGCU	262	AAGCAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCACAU	7662
1047	GUGGAUUAU U CUGCUUA	263	UAAAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUCCAC	7663
1048	UGGAUUAU C UGUUUA	264	UUAAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUCCA	7664
1053	AUUCUGCU U UAAUGCCU	265	AGGCAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGAAU	7665
1054	UUCUGCUU U AAUGCCU	266	AAGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCAGAA	7666
1055	UCUGCUUU A AUGCCUU	267	AAAGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCAGA	7667
1062	UAAUGCCU U UUAUGCA	268	UGCAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAUUA	7668
1063	AAUGCCUU U AUAUGCAU	269	AUGCAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCAU	7669
1064	AUGCCUUU A UAUGCAUG	270	CAUGCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGCAU	7670
1066	GCCUUUAU A UGCAUGCA	271	UGCAUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAAGGC	7671
1076	GCAUGCAU A CAAGCAA	272	UUUGCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAUGC	7672
1092	AACAGGCU U UUAUUUC	273	GAAAGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCUGU	7673
1093	ACAGGCUU U UACUUUCU	274	AGAAAGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCUGU	7674
1094	CAGGCUUU U ACUUUCUC	275	GAGAAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCUG	7675
1095	AGGCUUUU A CUUUCUCG	276	CGAGAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGCCU	7676
1098	CUUUUACU U UUCGCCA	277	UGGCGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAAAG	7677
1099	UUUUACUU U CUGCCAA	278	UUGGCGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUAAAA	7678
1100	UUUACUUU C UCGCCAA	279	GUUGGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUAAA	7679
1102	UACUUUCU C GCCAACUU	280	AAGUUGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAAGUA	7680
1110	CGCCAAU U ACAAGGCC	281	GGCCUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGGCG	7681
1111	GCCAAU U CAAGGCCU	282	AGGCCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUGGC	7682
1120	CAAGGCCU U UCUAAGUA	283	UACUUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCUUG	7683

1121	AAGGCCUU U CUAAGUAA	284	UUACUUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCCUU	7684
1122	AGGCCUUU C UAAGUAAA	285	UUUACUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGCCU	7685
1124	GCCUUUCU A AGUAAACA	286	UGUUUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAAGGC	7686
1128	UUCUAAGU A AACAGUAA	287	AUACUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUUAGAA	7687
1135	UAAACAGU A UGUGAACC	288	GGUUCACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGUUUA	7688
1145	GUGAACCU U UACCCCGU	289	ACGGGGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUCAC	7689
1146	UGAACCUU U ACCCCGUU	290	AACGGGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGUUCA	7690
1147	GAACCUUU A CCCCUGU	291	CAACGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGUUC	7691
1154	UACCCCGU U GCUCGGCA	292	UGCCGAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGGUA	7692
1158	CCGUUGCU C GGCAACGG	293	CCGUUGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAACGG	7693
1173	GGCUGGU C UAUGCCAA	294	UUGGCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAGGCC	7694
1175	CCUGGUCU A UGCCAAGU	295	ACUUGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCAGG	7695
1186	CCAAGUGU U UGCGACG	296	CGUCAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACUUGG	7696
1187	CAAGUGUU U GCUGACGC	297	GCGUCAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACUUG	7697
1209	CCACUGGU U GGGGCUUG	298	CAAGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAGUGG	7698
1216	UUGGGGCU U GGCAUAG	299	CUAUGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCCAA	7699
1223	UUGGCCAU A GGCAUCA	300	UGAUGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGCCAA	7700
1230	UAGGCCAU C AGCGCAUG	301	CAUGCGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGCCUA	7701
1249	UGGAACCU U UGUGUCUC	302	GAGACACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUCCA	7702
1250	GGAACCUU U GUGUCUCC	303	GGAGACAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGUUCC	7703
1255	CUUUGUGU C UCCUCUGC	304	GCAGAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACAAAG	7704
1257	UUGUGUCU C CUCUGCCG	305	CGGCAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACACAA	7705
1260	UGUCUCU C UGCCGAUC	306	GAUCGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGACA	7706
1268	CUGCCGAU C CAUACCGC	307	GCGGUUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCGGCAG	7707
1272	CGAUCCAU A CCGCGGAA	308	UUCGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGAUCG	7708
1283	GCGGAACU C CUAGCCGC	309	GCGGCUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCGC	7709
1286	GAACUCCU A GCCGCUUG	310	CAAGCGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGUUC	7710
1293	UAGCCGCU U GUUUUGCU	311	AGCAAAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGGCUA	7711
1296	CCGCUUGU U UUGCUCGC	312	GCGAGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAGCGG	7712
1297	CGCUUGUU U UGUCGCA	313	UGCGAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAAGCG	7713
1298	GCUUGUUU U GCUCGCAG	314	CUGCGAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACAAGC	7714
1302	GUUUUGCU C GCAGCAGG	315	CCUGCUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAAAAC	7715
1312	CAGCAGGU C UGGGGCAA	316	UUGCCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUGCUG	7716
1325	GCAAAACU C AUCGGGAC	317	GUCCCGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUUGC	7717
1328	AAACUCAU C GGGACUGA	318	UCAGUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAGUUU	7718
1341	CUGACAAU U CUGUCGUG	319	CACGACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGUCAG	7719
1342	UGACAAU C UGUCGUGC	320	GCACGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGUCA	7720
1346	AAUUCUGU C GUGCUCUC	321	GAGAGCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGAAUU	7721
1352	GUCGUGCU C UCCCGCAA	322	UUGCGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCACGAC	7722
1354	CGUGCUCU C CCGCAAAU	323	AUUUGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGCACG	7723
1363	CCGCAAAU A UACAUCAU	324	AUGAUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUGCGG	7724
1365	GCAAAUUAU A CAUCAUUU	325	AAAUUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUUUGC	7725
1369	AUAUACAU C AUUCCAU	326	AUGGAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUAUUA	7726
1372	UACAUCAU U UCCAUGGC	327	GCCAUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUGUA	7727
1373	ACAUCAUU U CCAUGGCU	328	AGCCAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGAUGU	7728
1374	CAUCAUUU C CAUGGCUG	329	CAGCCAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUGAUG	7729
1385	UGGUCUGU A GGCUGUGC	330	GCACAGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGCCA	7730
1406	AACUGGAU C CUACGCGG	331	CCGCGUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCAGUU	7731
1409	UGGAUCCU A CGCGGGAC	332	GUCCCGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAUCCA	7732
1420	CGGGACGU C CUUUGUUU	333	AAACAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUCCCG	7733
1423	GACGUCCU U UGUUUACG	334	CGUAAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGACGUC	7734

1424	ACGUCCUU U GUUUACGU	335	ACGUAAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGACGU	7735
1427	UCCUUUGU U UACGUCCC	336	GGGACGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAGGA	7736
1428	CCUUUGUU U ACGUCCCG	337	CGGGACGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAAAGG	7737
1429	CUUUUGUU A CGUCCCGU	338	ACGGGACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACAAAG	7738
1433	GUUUACGU C CCGUCGGC	339	GCCGACGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUAAAC	7739
1438	CGUCCCGU C GCGCUGA	340	UCAGCGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGACG	7740
1449	CGCUGAAU C CCGCGGAC	341	GUCCGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCAGCG	7741
1465	CGACCCCU C CCGGGGCC	342	GGCCCCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGUCG	7742
1477	GGGCCGCU U GGGGCUCU	343	AGAGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGGCC	7743
1484	UUGGGGCU C UACCGCCC	344	GGGCGGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCCAA	7744
1486	GGGGCUCU A CCGCCCGC	345	GCGGCGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGCCCC	7745
1496	CGCCCGCU U CUCCGCCU	346	AGGCGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGGGCG	7746
1497	GCCCGCUU C UCCGCCUA	347	UAGGCGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCGGGC	7747
1499	CCGCUUCU C CGCUAAU	348	AAUAGGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGCGG	7748
1505	CUCCGCCU A UUGUACCG	349	CGGUACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCGGAG	7749
1507	CCGCCUAU U GUACCGAC	350	GUCGGUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGGCGG	7750
1510	CCUAUUGU A CCGACCGU	351	ACGGUCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAUAGG	7751
1519	CCGACCGU C CACGGGGC	352	GCCCCGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGUCGG	7752
1534	GCGCACCU C UCUUACG	353	CGUAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUGCGC	7753
1536	GCACCUCU C UUUACGCG	354	CGCGUAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGGUGC	7754
1538	ACCUCUCU U UACGCGGA	355	UCCGCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGAGGU	7755
1539	CCUCUCUU U ACGCGGAC	356	GUCCGCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAGAGG	7756
1540	CUCUCUUU A CGCGGACU	357	AGUCCGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAGAG	7757
1549	CGCGGACU C CCCGUCUG	358	CAGACGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCGCG	7758
1555	CUCCCCGU C UGUGCCUU	359	AAGGCACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGGAG	7759
1563	CUGUGCCU U CUAUCUG	360	CAGAUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCACAG	7760
1564	UGUGCCUU C UCAUCUGC	361	GCAGAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCACA	7761
1566	UGCCUUCU C AUCUGCCG	362	CGGCAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGGCA	7762
1569	CUUCUCAU C UGCGGAC	363	GUCCGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAGAAG	7763
1588	UGUGCACU U CGUUCAC	364	GUGAAGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGCACA	7764
1589	GUGCACUU C GCUUACC	365	GGUGAAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUGCAC	7765
1593	ACUUCGCU U CACCUCUG	366	CAGAGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGAAGU	7766
1594	CUUCGCUU C ACCUCUGC	367	GCAGAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCGAAG	7767
1599	CUUCACCU C UGCACGUC	368	GACGUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUGAAG	7768
1607	CUGCACGU C GCAUGGAG	369	CUCCAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUGCAG	7769
1651	CCCAAGGU C UUGCAUAA	370	UUAUGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUUGGG	7770
1653	CAAGGUCU U GCAUAAGA	371	UCUUAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCUUG	7771
1658	UCUUGCAU A AGAGGACU	372	AGUCCUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAAGA	7772
1667	AGAGGACU C UUGGACUU	373	AAGUCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCUCU	7773
1669	AGGACUCU U GGACUUUC	374	GAAAGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGUCCU	7774
1675	CUUGGACU U UCAGCAAU	375	AUUGCUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCAAG	7775
1676	UUGGACUU U CAGCAUUG	376	CAUUGCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUCCAA	7776
1677	UGGACUUU C AGCAAUGU	377	ACAUUGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUCCA	7777
1686	AGCAAUGU C AACGACCG	378	CGGUCGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUUGCU	7778
1699	ACCGACCU U GAGGCAUA	379	UAUGCCUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUCGGU	7779
1707	UGAGGCAU A CUUCAAG	380	CUUUGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCCUCA	7780
1710	GGCAUACU U CAAAGACU	381	AGUCUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAUGCC	7781
1711	GCAUACUU C AAAGACUG	382	CAGUCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUAUGC	7782
1725	CUGUGUGU U UAAUGAGU	383	ACUCAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACACAG	7783
1726	UGUGUGUU U AAUGAGUG	384	CACUCAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACACA	7784
1727	GUGUGUUU A AUGAGUGG	385	CCACUCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACACAC	7785

1743	GGAGGAGU U GGGGAGG	386	CCUCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCCUCC	7786
1756	GAGGAGGU U AGGUUAAA	387	UUUAACCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUCCUC	7787
1757	AGGAGGUU A GGUUAAAG	388	CUUUAACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCUCCU	7788
1761	GGUUAGGU U AAAGGUCU	389	AGACCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUAACC	7789
1762	GUUAGGUU A AAGGUCUU	390	AAGACCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCUAAC	7790
1768	UUAAAGGU C UUUUACU	391	AGUACAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUUUAA	7791
1770	AAAGGUCU U UGUACUAG	392	CUAGUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCUUU	7792
1771	AAGGUCUU U GUACUAGG	393	CCUAGUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACCUU	7793
1774	GUCUUUGU A CUAGGAGG	394	CCUCCUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAGAGAC	7794
1777	UUUGUACU A GGAGGCUG	395	CAGCCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUACAAA	7795
1787	GAGGCUGU A GGCAUAAA	396	UUUAUGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGCCUC	7796
1793	GUAGGCAU A AAUUGGUG	397	CACCAAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCCUAC	7797
1797	GCAUAAAU U GGUUGUUU	398	AACACACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUAUGC	7798
1805	UGGUGUGU U CACCAGCA	399	UGCUGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACACCA	7799
1806	GGUGUGUU C ACCAGCAC	400	GUGCUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACACC	7800
1824	AUGCAACU U UUUACCUU	401	AGGUGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGCAU	7801
1825	UGCAACUU U UUCACCUC	402	GAGGUGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUGCA	7802
1826	GCAACUUU U UCACCUCU	403	AGAGGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUUGC	7803
1827	CAACUUUU U CACCUCUG	404	CAGAGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGUUG	7804
1828	AACUUUUU C ACCUCUGC	405	GCAGAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGUUU	7805
1833	UUUCACCU C UGCCUAAU	406	AUUAGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUGAAA	7806
1839	CUCUGCCU A AUCAUUC	407	GAGAUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAGAG	7807
1842	UGCCUAAU C AUCUCAUG	408	CAUGAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAGGCA	7808
1845	CUAAUCAU C UCAUGUUC	409	GAACAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUUAG	7809
1847	AAUCAUCU C AUGUUCU	410	AUGAACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGAUU	7810
1852	UCUCAUGU U CAUGUCCU	411	AGGACAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUGAGA	7811
1853	CUCAUGUU C AUGUCCUA	412	UAGGACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUAGAG	7812
1858	GUUCAUGU C CUACUGUU	413	AACAGUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUGAAC	7813
1861	CAUGUCCU A CUGUUCAA	414	UUGAACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGACAUG	7814
1866	CCUACUGU U CAAGCCUC	415	GAGGCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUAGG	7815
1867	CUACUGUU C AAGCCUCC	416	GGAGGCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAGUAG	7816
1874	UCAAGCCU C CAAGCUGU	417	ACAGCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCUUGA	7817
1887	CUGUGCCU U GGGUGGCU	418	AGCCACCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCACAG	7818
1896	GGGUGGCU U UGGGGCAU	419	AUGCCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCACCC	7819
1897	GGUGGCUU U GGGGCAUG	420	CAUGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCACC	7820
1911	AUGGACAU U GACCCGUA	421	UACGGGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCCAU	7821
1919	UGACCCGU A UAAAGAAU	422	AUUCUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGUCA	7822
1921	ACCCGUAU A AAGAAUUU	423	AAAUUCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACGGGU	7823
1928	UAAAGAAU U UGGAGCUU	424	AAGCUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCUUUA	7824
1929	AAAGAAUU U GGAGCUUC	425	GAAGCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUCUUU	7825
1936	UUGGAGCU U CUGUGGAG	426	CUCCACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCUCCAA	7826
1937	UGGAGCUU C UGUGGAGU	427	ACUCCACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCUCCA	7827
1946	UGUGGAGU U ACUCUCUU	428	AAGAGAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCCACA	7828
1947	GUGGAGUU A CUCUCUUU	429	AAAGAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACUCCAC	7829
1950	GAGUUACU C UCUUUUUU	430	AAAAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAACUC	7830
1952	GUUACUCU C UUUUUUGC	431	GCAAAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGUAAAC	7831
1954	UACUCUCU U UUUUGCCU	432	AGGCAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGAGUA	7832
1955	ACUCUCUU U UUUGCCUU	433	AAGGCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAGAGU	7833
1956	CUCUCUUU U UUGCCUUC	434	GAAGGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAGAG	7834
1957	UCUCUUUU U UGCCUUCU	435	AGAAGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGAGA	7835
1958	CUCUUUUU U GCCUUCUG	436	CAGAAGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAAGAG	7836

1963	UUUUGCCU U CUGACUUC	437	GAAGUCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAAAA	7837
1964	UUUGCCUU C UGACUUCU	438	AGAAGUCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCAAA	7838
1970	UUCUGACU U CUUCCUU	439	AAGGAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCAGAA	7839
1971	UCUGACUU C UUCCUUC	440	GAAGGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUCAGA	7840
1973	UGACUUCU U UCCUUCUA	441	UAGAAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGUCA	7841
1974	GACUUCUU U CCUUCUUA	442	AUAGAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAGUC	7842
1975	ACUUCUUU C CUUCUUAU	443	AAUAGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAAGU	7843
1978	UCUUUCCU U CUAUUCGA	444	UCGAAUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAAAGA	7844
1979	CUUUCUU C UAUUCGAG	445	CUCGAAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGAAAG	7845
1981	UUCUUCU A UUCGAGAU	446	AUCUCGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGGAA	7846
1983	CCUUCUAU U CGAGAUUC	447	AGAUCUCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGAAGG	7847
1984	CUUCUAUU C GAGAUUC	448	GAGAUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAGAAG	7848
1990	UUCGAGAU C UCCUCGAC	449	GUCGAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUCGAA	7849
1992	CGAGAUUC C CUCGACAC	450	GUGUCGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUCUCG	7850
1995	GAUCUCCU C GACACCGC	451	GCGGUGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGAUC	7851
2006	CACCGCCU C UGCUCUGU	452	ACAGAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCGGUG	7852
2011	CCUCUGCU C UGUUUCGG	453	CCGAUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGAGG	7853
2015	UGCUCUGU A UCGGGGGG	454	CCCCCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGAGCA	7854
2017	CUCUGUAU C GGGGGGCC	455	GGCCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACAGAG	7855
2027	GGGGGCCU U AGAGUCUC	456	GAGACUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCCCC	7856
2028	GGGGCCU A GAGUCUCC	457	GGAGACUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCCCC	7857
2033	CUUAGAGU C UCCGGAAC	458	GUUCCGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCUAAG	7858
2035	UAGAGUCU C CGGAACAU	459	AUGUUCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACUCUA	7859
2044	CGGAACAU U GUUCACCU	460	AGGUGAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCCG	7860
2047	AACAUUGU U CACCUCAC	461	GUGAGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAUUU	7861
2048	ACAUUGU C ACCUCACC	462	GGUGAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAAUGU	7862
2053	GUUCACCU C ACCAUACG	463	CGUAUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUGAAC	7863
2059	CUCACCAU A CGGCACUC	464	GAGUGCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGUGAG	7864
2067	ACGGCACU C AGGCAAGC	465	GCUUGCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGCCGU	7865
2077	GGCAAGCU A UUCUGUGU	466	ACACAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCUUGCC	7866
2079	CAAGCUAU U CUGUGUUG	467	CAACACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGCUUG	7867
2080	AAGCUAUU C UGUGUUGG	468	CCAACACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAGCUU	7868
2086	UUCUGUGU U GGGGUGAG	469	CUCACCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACAGAA	7869
2096	GGGUGAGU U GAUGAAUC	470	GAUUAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCACCC	7870
2104	UGAUGAAU C UAGCCACC	471	GGUGGCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCAUCA	7871
2106	AUGAAUCU A GCCACCUG	472	CAGGUGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUCAU	7872
2125	UGGGAAGU A AUUUGGAA	473	UUCCAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCCCCA	7873
2128	GAAGUAAU U UGGAAGAU	474	AUCUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUACUUC	7874
2129	AAGUAAU U GGAAGAUC	475	GAUCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUACUU	7875
2137	UGGAAGAU C CAGCAUCC	476	GGAUGCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUCCA	7876
2144	UCCAGCAU C CAGGGAU	477	AUUCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCUGGA	7877
2153	CAGGGAU U AGUAGUCA	478	UGACUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCCUG	7878
2154	AGGGAUU A GUAGUCAG	479	CUGACUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUCCCU	7879
2157	GAAUAGU A GUCAGCUA	480	UAGCUGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUAAUUC	7880
2160	UUAGUAGU C AGCUAUGU	481	ACAUAGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUACUAA	7881
2165	AGUCAGCU A UGUCAACG	482	CGUUGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCUGACU	7882
2169	AGCUAUGU C AACGUUAA	483	UUAACGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUAGCU	7883
2175	GUCAACGU U AAUUGGG	484	CCCAUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUUGAC	7884
2176	UCAACGUU A AUUUGGGC	485	GCCCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACGUUGA	7885
2179	ACGUAAU A UGGGCCUA	486	UAGGCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAACGU	7886
2187	AUGGGCCU A AAAUUCAG	487	CUGAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCCAU	7887

2193	CUAAAAAU C AGACAACU	488	AGUUGUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUUAG	7888
2202	AGACAACU A UUGUGGUU	489	AACCACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGUCU	7889
2204	ACAACUUAU U GUGGUUUC	490	GAAACCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGUUGU	7890
2210	AUUGUGGU U UCACAUUU	491	AAAUUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCACAAU	7891
2211	UUGUGGUU U CACAUUUC	492	GAAAUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCACAA	7892
2212	UGUGGUUU C ACAUUUCC	493	GGAAUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACCACA	7893
2217	UUUCACAU U UCCUGUCU	494	AGACAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUGAAA	7894
2218	UUCACAUU U CCUGUCUU	495	AAGACAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGUGAA	7895
2219	UCACAUUU C CUGUCUUA	496	UAAGACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUGUGA	7896
2224	UUUCCUGU C UUACUUUU	497	AAAAGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGGAAA	7897
2226	UCCUGUCU U ACUUUUUG	498	CCAAAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACAGGA	7898
2227	CCUGUCUU A CUUUUGGG	499	CCCAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACAGG	7899
2230	GUCUUAU U UUGGGCGA	500	UCGCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAGAC	7900
2231	UCUUAUUU U UGGGCGAG	501	CUCGCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUAAGA	7901
2232	CUUACUUU U GGGCGAGA	502	UCUCGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUAAG	7902
2247	GAAACUGU U CUUGAAUA	503	UAUUCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUUUC	7903
2248	AAACUGUU C UUGAAUAU	504	AUAUCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAGUUU	7904
2250	ACUGUUCU U GAAUAUUU	505	AAAUUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAACAGU	7905
2255	UCUUGAAU A UUUGGUGU	506	ACACCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCAAGA	7906
2257	UGAAUAU U UGGUGUCU	507	AGACACCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUCAA	7907
2258	UGAAUAU U GGUGUCUU	508	AAGACACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUUA	7908
2264	UUUGGUGU C UUUUGGAG	509	CUCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACCAA	7909
2266	UGGUGUCU U UUGGAGUG	510	CACUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACACCA	7910
2267	GGUGUCUU U UGGAGUGU	511	ACACUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACACC	7911
2268	GUGUCUUU U GGAGUGUG	512	CACACUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGACAC	7912
2280	GUGUGGAU U CGCACUCC	513	GGAGUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCACAC	7913
2281	UGUGGAU C GCACUCCU	514	AGGAGUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUCCACA	7914
2287	UUCGCACU C CUCCUGCA	515	UGCAGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGCGAA	7915
2290	GCACUCCU C CUGCAUAU	516	AUAUGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGUGC	7916
2297	UCCUGCAU A UAGACCAC	517	GUGGUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAGGA	7917
2299	CUGCAUAU A GACCACCA	518	UGGUGGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUGCAG	7918
2317	AUGCCCCU A UCUAUCA	519	UGAUAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGCAU	7919
2319	GCCCCUUAU C UUAUCAAC	520	GUUGAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGGGGC	7920
2321	CCCUAUCU U AUCAACAC	521	GUGUUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUAGGG	7921
2322	CCUAUCUU A UCAACACU	522	AGUGUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUAGG	7922
2324	UAUCUUUAU C AACACUUC	523	GAAGUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAGAU	7923
2331	UCAACACU U CCGAAAC	524	GUUUCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGUUGA	7924
2332	CAACACUU C CGGAAACU	525	AGUUUCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUGUUG	7925
2341	CGGAAACU A CUGUUGUU	526	AACAACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUCCG	7926
2346	ACUACUGU U GUUAGACG	527	CGUCUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUAGU	7927
2349	ACUGUUGU U AGACGAAG	528	CUUCGUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAACAGU	7928
2350	CUGUUGUU A GACGAAGA	529	UCUUCGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACAG	7929
2366	AGGCAGGU C CCUAGAA	530	UUCUAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUGCCU	7930
2371	GGUCCCCU A GAAGAAGA	531	UCUUCUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGACC	7931
2383	GAAGAACU C CCUCGCCU	532	AGGCGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUCUUC	7932
2387	AACUCCCU C GCCUCGCA	533	UGCAGGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGAGUU	7933
2392	CCUCGCCU C GCAGACGA	534	UCGUCGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCGAGG	7934
2405	ACGAAGGU C UCAAUCGC	535	GCGAUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUUCGU	7935
2407	GAAGGUCU C AAUCGCCG	536	CGGCGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCUUC	7936
2411	GUCUCAAU C GCCGCGUC	537	GACGCGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGAGAC	7937
2419	CGCCGCGU C GCAGAAGA	538	UCUUCUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGCGGCG	7938

2429	CAGAAGAU C UCAAUCUC	539	GAGAUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUUCUG	7939
2431	GAAGAUCU C AAUCUCGG	540	CCGAGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUCUUC	7940
2435	AUCUCAAU C UCGGGAU	541	AUUCCCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGAGAU	7941
2437	CUCAAUUC C GGGAAUCU	542	AGAUUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUGAG	7942
2444	UCGGGAU C UCAAUGUU	543	AACAUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCCCGA	7943
2446	GGGAUUCU C AAUGUUAG	544	CUAACAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUCCC	7944
2452	CUCAUGU U AGUAUUC	545	GGAAUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUUGAG	7945
2453	UCAAUGU A GUUAUCCU	546	AGGAAUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUUGA	7946
2456	AUGUUAGU A UUCUUGG	547	CCAAGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUAACAU	7947
2458	GUUAGUUA U CCUUGGAC	548	GUCCAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACUAAC	7948
2459	UUAGUUAU C CUUGGACA	549	UGUCCAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUACUAA	7949
2462	GUUUUCCU U GGACACAU	550	AUGUGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAAUAC	7950
2471	GGACACAU A AGGUGGGA	551	UCCCACCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUGUCC	7951
2484	GGGAAACU U UACGGGGC	552	GCCCCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUCCC	7952
2485	GGAAACUU U ACGGGGCU	553	AGCCCCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUUCC	7953
2486	GAAACUUU A CGGGGCUU	554	AAGCCCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUUUC	7954
2494	ACGGGGCU U UAUUCUUC	555	GAAGAAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCCGU	7955
2495	CGGGGCUU U AUUCUUCU	556	AGAAGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCCCG	7956
2496	GGGGCUUU A UUCUUCUA	557	UAGAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCCC	7957
2498	GGCUUUUA U CUUCUACG	558	CGUAGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAAGCC	7958
2499	GCUUUUAU C UUCUACGG	559	CCGUAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAAAGC	7959
2501	UUUAUUCU U CUACGGUA	560	UACCGUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAUAAA	7960
2502	UUAUUCUU C UACGGUAC	561	GUACCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAUAA	7961
2504	AUUCUUCU A CGGUACCU	562	AGGUACCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGAAU	7962
2509	UCUACGGU A CCUUGCUU	563	AAGCAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCGUAGA	7963
2513	CGGUACCU U GCUUUAU	564	AUUAAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUACCG	7964
2517	ACCUUGCU U UAAUCCUA	565	UAGGAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAAGGU	7965
2518	CCUUGCUU U AAUCCUAA	566	UUAGGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCAAGG	7966
2519	CUUGCUUU A AUCCUAAA	567	UUUAGGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCAAG	7967
2522	GCUUUAU C CUAAAUGG	568	CCAUUUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAAAGC	7968
2525	UUAUCCU A AAUGGCAA	569	UUGCCAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAUUA	7969
2537	GGCAAACU C CUUCUUUU	570	AAAAGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUGCC	7970
2540	AAACUCCU U CUUUUCCU	571	AGGAAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGUUU	7971
2541	AACUCCUU C UUUUCCUG	572	CAGGAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGAGUU	7972
2543	CUCCUUCU U UUCUGAC	573	GUCAGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGGAG	7973
2544	UCCUUCUU U UCCUGACA	574	UGUCAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAGGA	7974
2545	CCUUCUUU U CCUGACAU	575	AUGUCAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAAGG	7975
2546	CUUCUUUU C CUGACAUU	576	AAUGUCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGAAG	7976
2554	CCUGACAU U CAUUUGCA	577	UGCAAAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCAGG	7977
2555	CUGACAUU C AUUUGCAG	578	CUGCAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGUCAG	7978
2558	ACAUUCAU U UGCAGGAG	579	CUCCUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAAUGU	7979
2559	CAUUCAU U GCAGGAGG	580	CCUCCUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGAAUG	7980
2572	GAGGACAU U GUUGAUAG	581	CUAUCAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCCUC	7981
2575	GACAUUGU U GAUAGAUG	582	CAUCUAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAUGUC	7982
2579	UUGUUGAU A GAUGUAAG	583	CUUACAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCAACAA	7983
2585	AUAGAUGU A AGCAAUUU	584	AAAUUGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUCUAU	7984
2592	UAAGCAAU U UGUGGGGC	585	GCCCCACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGCUUA	7985
2593	AAGCAAUU U GUGGGGCC	586	GGCCCCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGCUU	7986
2605	GGGCCCCU U ACAGUAAA	587	UUUACUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGCC	7987
2606	GGCCCCUU A CAGUAAAU	588	AUUUACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGGCC	7988
2611	CUUACAGU A AAUGAAAA	589	UUUUCAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGUAAG	7989

2629	AGGAGACU U AAAUUAAC	590	GUUAAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCUCCU	7990
2630	GGAGACUU A AAUUAACU	591	AGUUAAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUCUCC	7991
2634	ACUUAUUU U AACUAUGC	592	GCAUAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUAAAGU	7992
2635	CUUAAAUU A ACUAUGCC	593	GGCAUAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUAAG	7993
2639	AAUUAACU A UGCCUGCU	594	AGCAGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUAUU	7994
2648	UGCCUGCU A GGUUUUAU	595	AUAAAACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGGCA	7995
2652	UGCUAGGU U UUAUCCCA	596	UGGGAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUAGCA	7996
2653	GCUAGGUU U UAUCCCAA	597	UUGGGAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCUGAG	7997
2654	CUAGGUUU U AUCCCAAU	598	AUUGGGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACCUAG	7998
2655	UAGGUUUU A UCCCAAUG	599	CAUUGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAACCUA	7999
2657	GGUUUUUA C CCAAUGUU	600	AACAUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAAACC	8000
2665	CCCAAUGU U ACUAAUAU	601	UAUUUAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUUGGG	8001
2666	CCAAUGUU A CUAAUAU	602	AUAUUUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUUGG	8002
2669	AUGUUACU A AAUAUUUG	603	CAAAUAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAACAU	8003
2673	UACUAAAU A UUUGCCCU	604	AGGGCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUAGUA	8004
2675	CUAAUAU U UGCCCUUA	605	UAAGGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUAG	8005
2676	UAAUAUU U GCCCUUAG	606	CUAAGGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUUUA	8006
2682	UUUGCCCU U AGAUAAAG	607	CUUUUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGCAAA	8007
2683	UUGCCCUU A GAUAAAGG	608	CCUUUAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGCAA	8008
2687	CCUUAAGU A AAGGGAUC	609	GAUCCCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUAAGG	8009
2695	AAAGGGAU C AAACCGUA	610	UACGGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCUUU	8010
2703	CAAACCGU A UUAUCCAG	611	CUGGAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGUUUG	8011
2705	AACCGUAU U AUCCAGAG	612	CUCUGGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACGGUU	8012
2706	ACCGUAUU A UCCAGAGU	613	ACUCUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUACGGU	8013
2708	CGUAUUUA C CAGAGUAU	614	AUACUCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAUACG	8014
2715	UCCAGAGU A UGUAGUUA	615	UAACUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCUGGA	8015
2719	GAGUAUGU A GUUAUAUA	616	UGAUUAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUACUC	8016
2722	UAUGUAGU U AAUCAUUA	617	UAAUGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUACAU	8017
2723	AUGUAGUU A AUCAUUAC	618	GUAAUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACUACAU	8018
2726	UAGUUAUU C AUUACUUC	619	GAAGUAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAACUA	8019
2729	UUAUUAU U ACUCCAG	620	CUGGAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUUAA	8020
2730	UAAUCAUU A CUUCCAGA	621	UCUGGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGAUUA	8021
2733	UCAUUACU U CCAGACGC	622	GCGUCUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAUGA	8022
2734	CAUUACUU C CAGACGCG	623	CGCUCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUAAUG	8023
2747	CGCGACAU U AUUUACAC	624	GUGUAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCGCG	8024
2748	GCGACAUU A UUUACACA	625	UGUGUAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGUCGC	8025
2750	GACAUUAU U UACACACU	626	AGUGUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAUGUC	8026
2751	ACAUUAUU U ACACACUC	627	GAGUGUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUUGU	8027
2752	CAUUAUUU A CACACUCU	628	AGAGUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUAUUG	8028
2759	UACACACU C UUUGGAAG	629	CUUCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGUGUA	8029
2761	CACACUCU U UGGAAGGC	630	GCCUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGUGUG	8030
2762	ACACUCUU U GGAAGGCG	631	CGCCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAGUGU	8031
2776	GCGGGGAU C UUAUAUAA	632	UUAUAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCCGC	8032
2778	GGGGAUCU U AUUAUAAA	633	UUUUUAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUCCCC	8033
2779	GGGAUCUU A UUAUAAAG	634	CUUUUAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUCCC	8034
2781	GAUCUUUA A UAAAGAG	635	CUCUUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGAUC	8035
2783	UCUUUAUU A AAAGAGAG	636	CUCUCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAAGA	8036
2793	AAGAGAGU C CACACGUA	637	UACGUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCUCUU	8037
2801	CCACACGU A GCGCCUCA	638	UGAGGCGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUGUGG	8038
2808	UAGCGCCU C AUUUUGCG	639	CGCAAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCGCUA	8039
2811	CGCCUCAU U UUGCGGGU	640	ACCCGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAGGCG	8040

2812	GCCUCAUU U UGCGGGUC	641	GACCCGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGAGGC	8041
2813	CCUCAUUU U GCGGGUCA	642	UGACCCGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUGAGG	8042
2820	UUGCGGGU C ACCAUAUU	643	AAUAUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCGCAA	8043
2826	GUCACCAU A UUCUUGGG	644	CCCAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGUGAC	8044
2828	CACCAUAU U CUUGGGAA	645	UUCCCAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUGGUG	8045
2829	ACCAUAUU C UUGGGAAC	646	GUUCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUGGU	8046
2831	CAUAUUCU U GGGAACAA	647	UUGUCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAUAUG	8047
2843	AACAAGAU C UACAGCAU	648	AUGCUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUUGUU	8048
2845	CAAGAUUC A CAGCAUGG	649	CCAUGCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUCUUG	8049
2859	UGGGAGGU U GGUCUCC	650	GGAAGACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUCCCA	8050
2863	AGGUUGGU C UUCCAAAC	651	GUUUGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAACCU	8051
2865	GUUGGUCU U CCAAACCU	652	AGGUUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCAAC	8052
2866	UUGGUCUU C CAAACCUC	653	GAGGUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACCAA	8053
2874	CCAAACCU C GAAAAGGC	654	GCCUUUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUUGG	8054
2895	GGACAAAU C UUUCUGUC	655	GACAGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUGUCC	8055
2897	ACAAAUUC U UCUGUCCC	656	GGGACAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUUGU	8056
2898	CAAUUCUU U CUGUCCCC	657	GGGGACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUUUG	8057
2899	AAAUUCUU C UGUCCCCA	658	UGGGGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAUUU	8058
2903	CUUUCUGU C CCCAAUCC	659	GGAUUGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGAAAG	8059
2910	UCCCCAAU C CCUGGGGA	660	UCCCAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGGGGA	8060
2920	CCUGGGAU U CUUCCCCG	661	CGGGGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCAGG	8061
2921	CUGGGAUU C UUCCCCGA	662	UCGGGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUCCAG	8062
2923	GGGAUUCU U CCCC GAUC	663	GAUCGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAUCCC	8063
2924	GGAUUCUU C CCCGAUCA	664	UGAUCGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAUCC	8064
2931	UCCCCGAU C AUCAGUUG	665	CAACUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCGGGGA	8065
2934	CCGAUCAU C AGUUGGAC	666	GUCCAACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUCGG	8066
2938	UCAUCAGU U GGACCCUG	667	CAGGGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAUGA	8067
2950	CCCUGCAU U CAAAGCCA	668	UGGCUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAGGG	8068
2951	CCUGCAUU C AAAGCCAA	669	UUGGCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGCAGG	8069
2962	AGCCAACU C AGUAAAUC	670	GAUUUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGGCU	8070
2966	AACUCAGU A AAUCCAGA	671	UCUGGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAGUU	8071
2970	CAGUAAAU C CAGAUUGG	672	CCAAUCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUACUG	8072
2976	AUCCAGAU U GGGACCUC	673	GAGGUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUGGAU	8073
2984	UGGGACCU C AACCCGCA	674	UGCGGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUCCCA	8074
3037	GGGAGCAU U CGGGCCAG	675	CUGGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCUCCC	8075
3038	GGAGCAUU C GGGCCAGG	676	CCUGGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGCUCU	8076
3049	GCCAGGGU U CACCCUC	677	GAGGGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCUGGC	8077
3050	CCAGGGUU C ACCCUCU	678	GGAGGGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCCUGG	8078
3057	UCACCCCU C CCAUGGG	679	CCCAUGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGUGA	8079
3073	GGGACUGU U GGGGUGGA	680	UCCACCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUCCC	8080
3087	GGAGCCCU C ACGCUCAG	681	CUGAGCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGCUCU	8081
3093	CUCACGCU C AGGGCCUA	682	UAGGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGUGAG	8082
3101	CAGGGCCU A CUCACAAC	683	GUUGUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCUCG	8083
3104	GGCCUACU C ACAACUGU	684	ACAGUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAGGCC	8084
3123	CAGCAGCU C CUCCUCCU	685	AGGAGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCUGCUG	8085
3126	CAGCUCCU C CUCCUGCC	686	GGCAGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGCUG	8086
3129	CUCCUCCU C CUGCCUCC	687	GGAGGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGGAG	8087
3136	UCCUGCCU C CACCAAUC	688	GAUUGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAGGA	8088
3144	CCACCAAU C GGCAGUCA	689	UGACUGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGGUGG	8089
3151	UCGGCAGU C AGGAAGGC	690	GCCUUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGCCGA	8090
3165	GGCAGCCU A CUCCCUUA	691	UAAGGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCUGCC	8091

3168	AGCCUACU C CCUUAUCU	692	AGAUAAAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUAGGCU	8092
3172	UACUCCCU U AUCUCCAC	693	GUGGAGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGGAGUA	8093
3173	ACUCCCUU A UCUCACC	694	GGUGGAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGGGAGU	8094
3175	UCCCUUUAU C UCCACCUC	695	GAGGUGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUAAGGGA	8095
3177	CCUUAUCU C CACCUCUA	696	UAGAGGUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAUAAAGG	8096
3183	CUCCACCU C UAAGGGAC	697	GUGCCCUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGUGGAG	8097
3185	CCACCUCU A AGGGACAC	698	GUGUCCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAGGUGG	8098
3195	GGGACACU C AUCCUCAG	699	CUGAGGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUGUCCC	8099
3198	ACACUCAU C CUCAGGCC	700	GGCCUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUGAGUGU	8100
3201	CUCAUCCU C AGGCCAUG	701	CAUGGCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGAUGAG	8101

Input Sequence = AF100308. Cut Site = UH/.

Stem Length = 8 . Core Sequence = CUGAUGAG GCCGUUAGGC CGAA

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

Underlined region can be any X sequence or linker, as described herein.

TABLE VI: HUMAN HBV INOZYME AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	Inozyme	Seq ID
9	AACUCCAC C ACUUUCCA	702	UGGAAAGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGAGUU	8102
10	ACUCCACC A CUUUCAC	703	GUGGAAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGAGU	8103
12	UCCACCAC U UUCCACCA	704	UGGUGGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGUGGA	8104
16	CCACUUUC C ACCAAACU	705	AGUUUGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAGUGG	8105
17	CACUUUCC A CCAAACUC	706	GAGUUUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAAGUG	8106
19	CUUCCAC C AAACUCUU	707	AAGAGUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGAAAG	8107
20	UUUCCACC A AACUCUUC	708	GAAGAGUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGAAA	8108
24	CACCAAAC U CUUCAAGA	709	UCUUGAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUGGUG	8109
26	CCAAACUC U UCAAGAUC	710	GAUCUUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUUUGG	8110
29	AACUCUUC A AGAUCCCA	711	UGGGAUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGAGUU	8111
35	UCAAGAUC C CAGAGUCA	712	UGACUCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUCUUGA	8112
36	CAAGAUC C AGAGUCAG	713	CUGACUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUCUUG	8113
37	AAGAUC C A GAGUCAGG	714	CCUGACUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGAUCUU	8114
43	CCAGAGUC A GGGCCUG	715	CAGGGCCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACUCUGG	8115
48	GUCAGGGC C CUGUACUU	716	AAGUACAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUGAC	8116
49	UCAGGGCC C UGUACUUU	717	AAAGUACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCCUGA	8117
50	CAGGGCCC U GUACUUUC	718	GAAAGUAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCCUG	8118
55	CCUGUAC U UUCUGCU	719	AGCAGGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUACAGGG	8119
59	GUACUUUC C UGUGGUG	720	CACCAGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAGUAC	8120
60	UACUUUC U GUGGUGG	721	CCACCAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAAGUA	8121
63	UUUCCUGC U GGUGGCUC	722	GAGCCACC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGAAA	8122
70	CUGGUGGC U CCAGUUA	723	UGAACUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCACCAG	8123
72	GGUGGCUC C AGUUCAGG	724	CCUGAACU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCCACC	8124
73	GUGGCUC A GUUCAGGA	725	UCCUGAAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGCCAC	8125
78	UCCAGUUC A GGAACAGU	726	ACUGUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAACUGGA	8126
84	UCAGGAAC A GUGAGCCC	727	GGGCUCAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCCUGA	8127
91	CAGUGAGC C UGCUCAG	728	CUGAGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUCACUG	8128
92	AGUGAGCC C UGCUCAGA	729	UCUGAGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCUCACU	8129
93	GUGAGCCC U GCUCAGAA	730	UUCUGAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCUCAC	8130
96	AGCCUGC U CAGAAUAC	731	GUAUUCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGGCU	8131
98	CCUGCUC A GAAUACUG	732	CAGUAUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCAGGG	8132
105	CAGAAUAC U GUCUCUGC	733	GCAGAGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAUUCUG	8133
109	AUACUGUC U CUGCCAUA	734	UAUGGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAGUUA	8134
111	ACUGUCUC U GCCAUUAC	735	GAUAUGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGACAGU	8135
114	GUCUCUGC C AUUACUGC	736	GACGAUUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGAGAC	8136
115	UCUCUGCC A UAUCGUA	737	UGACGAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACAGAG	8137
123	AUAUCGUC A AUCUUAUC	738	GAUAAGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACGAUUA	8138
127	CGUCAAUC U UAUCGAAG	739	CUUCGAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUGACG	8139
138	UCGAAGAC U GGGGACCC	740	GGGUCCCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCUUCGA	8140
145	CUGGGGAC C CUGUACCG	741	CGGUACAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCCCAG	8141
146	UGGGGACC C UGUACCGA	742	UCGGUACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCCCCA	8142
147	GGGGACCC U GUACCGAA	743	UUCGGUAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGUCCCC	8143
152	CCUGUAC C GAACAUUG	744	CCAUGUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUACAGGG	8144
157	UACCGAAC A UGGAGAAC	745	GUUCUCCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCGGUA	8145
166	UGGAGAAC A UCGAUCA	746	UGAUGCGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCUCCA	8146
171	AACAUCGC A UCAGGACU	747	AGUCCUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAUGUU	8147

174	AUCGCAUC A GGACUCCU	748	AGGAGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUGCGAU	8148
179	AUCAGGAC U CCUAGGAC	749	GUCCUAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUCCUGAU	8149
181	CAGGACUC C UAGGACCC	750	GGGUCCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGUCCUG	8150
182	AGGACUCC U AGGACCCC	751	GGGGUCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAGUCCU	8151
188	CCUAGGAC C CCUGCUCG	752	CGAGCAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUCCUAGG	8152
189	CUAGGACC C CUGCUCGU	753	ACGAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUCCUAG	8153
190	UAGGACCC C UGCUCGUG	754	CACGAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGUCCUA	8154
191	AGGACCCC U GCUCGUGU	755	ACACGAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGGUCCU	8155
194	ACCCUGC U CGUGUUAU	756	GUAACACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICAGGGGU	8156
203	CGUGUUAU A GGCGGGGU	757	ACCCCGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUAACACG	8157
217	GGUUUUU U UGUUGACA	758	UGUCAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAAAACC	8158
225	UUGUUGAC A AAAAUCCU	759	AGGAUUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUCAACAA	8159
232	CAAAAUC C UCACAAUA	760	UAUUGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUUUUUG	8160
233	AAAAAUCC U CACAAUAC	761	GUAUUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAUUUUU	8161
235	AAAUCCUC A CAUACCA	762	UGGUUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGGAUUU	8162
237	AUCCUCAC A AUACCACA	763	UGUGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGAGGAU	8163
242	CACAAUAC C ACAGAGUC	764	GACUCUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUAUUGUG	8164
243	ACAAUACC A CAGAGUCU	765	AGACUCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUAUUGU	8165
245	AAUACCAC A GAGUCUAG	766	CUAGACUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGGUUUU	8166
251	ACAGAGUC U AGACUCGU	767	ACGAGUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACUCUGU	8167
256	GUCUAGAC U CGUGGUGG	768	CCACCACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUCUAGAC	8168
267	UGGUGGAC U UCUCUCAA	769	UUGAGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUCCACCA	8169
270	UGGACUUC U CUCAAUUU	770	AAAUUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAGUCCA	8170
272	GACUUCUC U CAUUUUUC	771	GAAAAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGAAGUC	8171
274	CUUCUCUC A AUUUUCUA	772	UAGAAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGAGAAG	8172
281	CAUUUUUC U AGGGGGAA	773	UUCCCCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAAAUUG	8173
291	GGGGGAAC A CCCGUGUG	774	CACACGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUCCCCC	8174
293	GGGAACAC C CGUGUGUC	775	GACACACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGUCCCC	8175
294	GGAAACAC C GUGUGUCU	776	AGACACAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUGUCC	8176
302	CGUGUGUC U UGGCCAAA	777	UUUGGCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACACACG	8177
307	GUCUUGGC C AAAAUUCG	778	CGAAUUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICCAAGAC	8178
308	UCUUGGCC A AAUUCGC	779	GCGAAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGCCAAGA	8179
317	AAAUUCGC A GUCCCAA	780	UUUGGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICGAAUUU	8180
321	UCGAGUC C CAAUUCUC	781	GAGAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACUGCGA	8181
322	CGCAGUCC C AAUUCUC	782	GGAGAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGACUGCG	8182
323	GCAGUCCC A AAUCUCCA	783	UGGAGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGACUGC	8183
328	CCCAAUUC U CCAGUCAC	784	GUGACUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUUUGGG	8184
330	CAAUUCUC C AGUCACUC	785	GAGUGACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGAUUUG	8185
331	AAUUCUC A GUCACUCA	786	UGAGUGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAGAUUU	8186
335	CUCCAGUC A CUCACCAA	787	UUGGUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACUGGAG	8187
337	CCAGUCAC U CACCAACC	788	GGUUGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGACUGG	8188
339	AGUCACUC A CCAACCUG	789	CAGGUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGUGACU	8189
341	UCACUCAC C AACCUGUU	790	AACAGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGAGUGA	8190
342	CACUCACC A ACCUGUUG	791	CAACAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUGAGUG	8191
345	UCACCAAC C UGUUGUCC	792	GGACAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUGGUGA	8192
346	CACCAACC U GUUGUCCU	793	AGGACAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUUGGUG	8193
353	CUGUUGUC C UCCAAUUU	794	AAAUUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACAACAG	8194
354	UGUUGUCC U CCAAUUUG	795	CAAAUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGACAACA	8195
356	UUGUCCUC C AAUUGUC	796	GACAAAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGGACAA	8196
357	UGUCCUCC A AUUUGUCC	797	GGACAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAGGACA	8197
365	AAUUGUC C UGGUUAUC	798	GAUAACCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACAAAUU	8198

366	AUUUGUCC U GGUUAUCG	799	CGAUAACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGACAAAU	8199
376	GUUAUCGC U GGAUGUGU	800	ACACAUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGAUAAC	8200
386	GAUGUGUC U GCGGCGUU	801	AACGCCGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACACAUC	8201
400	GUUUUAUC A UCUUCCUC	802	GAGGAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUAAAAC	8202
403	UUAUCAUC U UCCUCUGC	803	GCAGAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUGAUAA	8203
406	UCAUCUUC C UCUGCAUC	804	GAUGCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGAUGA	8204
407	CAUCUUC U CUGCAUCC	805	GGAUGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAGAUG	8205
409	UCUUCUC U GCAUCCUG	806	CAGGAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGAAGA	8206
412	UCCUCUGC A UCCUCUG	807	CAGCAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGAGGA	8207
415	UCUGCAUC C UGCUGCUA	808	UAGCAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUGCAGA	8208
416	CUGCAUCC U GCUGCUAU	809	AUAGCAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUGCAG	8209
419	CAUCCUGC U GCUAUGCC	810	GGCAUAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGAUG	8210
422	CCUGCUGC U AUGCCUCA	811	UGAGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGCAGG	8211
427	UGCUAUGC C UCAUCUUC	812	GAAGAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAUAGCA	8212
428	GCUAUGCC U CAUCUUCU	813	AGAAGAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAUAGC	8213
430	UAUGCCUC A UCUUCUUG	814	CAAGAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGCAUA	8214
433	GCCUCAUC U UCUUGUUG	815	CAACAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUAGGGC	8215
436	UCAUCUUC U UGUUGGUU	816	AACCAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGAUGA	8216
446	GUUGGUUC U UCUGGACU	817	AGUCCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAACCAAC	8217
449	GGUUCUUC U GGACUAUC	818	GAUAGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGAACC	8218
454	UUCUGGAC U AUCAAGGU	819	ACCUUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCAGAA	8219
458	GGACUAUC A AGGUAUGU	820	ACAUACCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUAGUCC	8220
470	UAUGUUGC C CGUUUGUC	821	GACAAACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAACUA	8221
471	AUGUUGCC C GUUUGUCC	822	GGACAAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAACAU	8222
479	CGUUUGUC C UCUAUUC	823	GAAUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACAAACG	8223
480	GUUUGUCC U CUAUUC	824	GGAAUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGACAAAC	8224
482	UUGUCCUC U AAUCCAG	825	CUGGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGACAA	8225
488	UCUAUUC C AGGAUCAU	826	AUGAUCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUAGA	8226
489	CUAAUUC A GGAUCAUC	827	GAUGAUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAUAG	8227
495	CCAGGAUC A UCAACAAC	828	GUUGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUCCUGG	8228
498	GGAUCAUC A ACAACCAG	829	CUGGUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUGAUCC	8229
501	UCAUCAAC A ACCAGCAC	830	GUGCUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGAUGA	8230
504	UCAACAAC C AGCACCGG	831	CCGUGUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGUUGA	8231
505	CAACAACC A GCACCGGA	832	UCCGGUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUUGUUG	8232
508	CAACCAGC A CCGACCA	833	UGGUCCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUGGUUG	8233
510	ACCAGCAC C GGACCAUG	834	CAUGGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCUGGU	8234
515	CACCGGAC C AUGCAAAA	835	UUUUGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCGGUG	8235
516	ACCGGACC A UGCAAAAC	836	GUUUUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCCGGU	8236
520	GACCAUGC A AAACUUC	837	GCAGGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAUGGUC	8237
525	UGCAAAAC C UGCACAAC	838	GUUGUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUUGCA	8238
526	GCAAAACC U GCACAACU	839	AGUUGUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUUUUGC	8239
529	AAACUUC A CAACUCCU	840	AGGAGUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGUUU	8240
531	ACCUGCAC A ACUCCUGC	841	GCAGGAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCAGGU	8241
534	UGCACAAC U CCUGCUCA	842	UGAGCAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGUGCA	8242
536	CACAACUC C UGCUCAAG	843	CUUGAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUUGUG	8243
537	ACAACUCC U GCUCAAGG	844	CCUUGAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGUUGU	8244
540	ACUCCUGC U CAAGGAAC	845	GUUCCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGAGU	8245
542	UCCUGCUC A AGGAACCU	846	AGGUCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGCAGGA	8246
549	CAAGGAAC C UCUAUGUU	847	AACAUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCCUUG	8247
550	AAGGAACC U CUAUGUUU	848	AAACAUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCCUUC	8248
552	GGAACCUC U AUGUUUCC	849	GGAAACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGUUCC	8249

560	UAUGUUUC C CUCAUGUU	850	AACAUGAG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAAACAU	8250
561	AUGUUUCC C UCAUGUUG	851	CAACAUGA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGAAACAU	8251
562	UGUUUCCC U CAUGUUGC	852	GCAACAUG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGGAAACA	8252
564	UUUCCUC A UGUUGCUG	853	CAGCAACA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAGGGAAA	8253
571	CAUGUUGC U GUACAAA	854	UUUUGUAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICAACAUG	8254
576	UGCUGUAC A AAACCUAC	855	GUAGGUUU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUACAGCA	8255
581	UACAAAAC C UACGGACG	856	CGUCCGUA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUUUUGUA	8256
582	ACAAAACC U ACGGACGG	857	CCGUCCGU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGUUUUGU	8257
595	ACGGAAAC U GCACCUGU	858	ACAGGUGC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUUUCGGU	8258
598	GAAACUGC A CCUGUAUU	859	AAUACAGG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICAGUUUC	8259
600	AACUGCAC C UGUUUCC	860	GGAAUACA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUGCAGUU	8260
601	ACUGCACC U GUUUUCCC	861	GGGAAUAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGUGCAGU	8261
608	CUGUAUUC C CAUCCCAU	862	AUGGGAUG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAAUACAG	8262
609	UGUAUUC C AUCCCAUC	863	GAUGGGAU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGAAUACA	8263
610	GUUUUCCC A UCCCAUCA	864	UGAUGGGA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGGAAUAC	8264
613	UCCCAUC C CAUCAUCU	865	AGAUGAUG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAUGGGAA	8265
614	UCCCAUCC C AUCAUCUU	866	AAGAUGAU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGAUGGGA	8266
615	CCCAUCCC A UCAUCUUG	867	CAAGAUGA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGAUGGGG	8267
618	AUCCCAUC A UCUUGGGC	868	GCCCAAGA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAUGGGAU	8268
621	CCAUCAUC U UGGGCUUU	869	AAAGCCCA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAUGAUGG	8269
627	UCUUGGGC U UUCGCAA	870	UUUGCGAA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICCCAAGA	8270
633	GCUUUCGC A AAAUACCU	871	AGGUUUUU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICGAAAGC	8271
640	CAAAUAC C UAUGGGAG	872	CUCCCAUA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUUUUUUG	8272
641	AAAUUACC U AUGGGAGU	873	ACUCCCAU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGUAUUUU	8273
654	GAGUGGGC C UCAGUCCG	874	CGGACUGA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICCCACUC	8274
655	AGUGGGCC U CAGUCCGU	875	ACGGACUG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGCCCACU	8275
657	UGGGCCUC A GUCCGUUU	876	AAACGGAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAGGCCCA	8276
661	CCUCAGUC C GUUUCUCU	877	AGAGAAAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IACUGAGG	8277
667	UCCGUUUC U CUUGGCUC	878	GAGCCAAG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAAACGGA	8278
669	CGUUUCUC U UGGCUCAG	879	CUGAGCCA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAGAAACG	8279
674	CUCUUGGC U CAGUUUAC	880	GUAAACUG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICCAAGAG	8280
676	CUUGGCUC A GUUUACUA	881	UAGUAAAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAGCCAAG	8281
683	CAGUUUAC U AGUGCCAU	882	AUGGCACU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUAAACUG	8282
689	ACUAGUGC C AUUUGUUC	883	GAACAAAU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICACUAGU	8283
690	CUAGUGCC A UUUGUUCA	884	UGAACAAA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGCACUAG	8284
698	AUUUGUUC A GUGGUUCG	885	CGAACAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAACAAAU	8285
713	CGUAGGGC U UUCCCCCA	886	UGGGGGAA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICCCUACG	8286
717	GGGCUUUC C CCCACUGU	887	ACAGUGGG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAAAGCCC	8287
718	GGCUUUC C CCACUGUC	888	GACAGUGG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGAAAGCC	8288
719	GCUUUCCC C CACUGUCU	889	AGACAGUG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGGAAAGC	8289
720	CUUUCCCC C ACUGUCUG	890	CAGACAGU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGGGAAAG	8290
721	UUUCCCCC A CUGUCUGG	891	CCAGACAG CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGGGGAAA	8291
723	UCCCCCAC U GUCUGGCU	892	AGCCAGAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUGGGGGA	8292
727	CCACUGUC U GGCUUUCA	893	UGAAAGCC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IACAGUGG	8293
731	UGUCUGGC U UUCAGUUA	894	UACUGAA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICCAGACA	8294
735	UGGCUUUC A GUUAUAUG	895	CAUAUAAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IAAAGCCA	8295
764	UUGGGGGC C AAGUCUGU	896	ACAGACUU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA ICCCCCAA	8296
765	UGGGGGCC A AGUCUGUA	897	UACAGACU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IGCCCCCA	8297
770	GCCAAGUC U GUACAACA	898	UGUUGUAC CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IACUUGGC	8298
775	GUCUGUAC A ACAUCUUG	899	CAAGAUGU CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUACAGAC	8299
778	UGUACAAC A UCUUGAGU	900	ACUCAAGA CUGAUGAG <u>GCCGUUAGGC</u>	CGAA IUUGUACA	8300

781	ACAACAUC U UGAGUCCC	901	GGGACUCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUGUUGU	8301
788	CUUGAGUC C CUUUAUGC	902	GCAUAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACUCAAG	8302
789	UUGAGUCC C UUUAUGCC	903	GGCAUAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGACUCAA	8303
790	UGAGUCCC U UUAUGCCG	904	CGGCAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGACUCA	8304
797	CUUUAUGC C GCUGUAC	905	GUAACAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICAUAAAG	8305
800	UAUGCCGC U GUUACCAA	906	UUGGUAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICGGCAUA	8306
806	GCUGUAC C AAUUUUCU	907	AGAAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUAACAGC	8307
807	CUGUACC A AUUUUCU	908	AAGAAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUAACAG	8308
814	CAAUUUUC U UUUGUCU	909	AAGACAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAAAUUG	8309
821	CUUUUGUC U UUGGGU	910	AUACCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACAAAAG	8310
832	GGGUUAUC A UUUAAACC	911	GGUUUAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUAUACCC	8311
840	AUUUAAAC C CUCACAAA	912	UUUGUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUUAAA	8312
841	UUUAAACC C UCACAAA	913	UUUUGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUUUAAA	8313
842	UUAAACCC U CACAAAAC	914	GUUUUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGUUUA	8314
844	AAACCCUC A CAAAACAA	915	UUGUUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGGGUU	8315
846	ACCCUCAC A AAACAAA	916	UUUUGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGAGGGU	8316
851	CACAAAAC A AAAAGAU	917	CAUCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUUUGUG	8317
869	GGAUUAUC C CUUAACU	918	AAGUUAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAUAUCC	8318
870	GAUAUUC C UUAACUUC	919	GAAGUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAUAUUC	8319
871	AUAUUCU C UUAACUUC	920	UGAAGUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGAUAU	8320
876	CCCUAAC U UCAUGGGA	921	UCCCAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUAAAGG	8321
879	UUAACUUC A UGGGAU	922	AUAUCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAGUUA	8322
906	GUUGGGGC A CAUUGCCA	923	UGGCAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICCCCAAC	8323
908	UGGGGCAC A UUGCCACA	924	UGUGGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGCCCA	8324
913	CACAUUGC C ACAGGAAC	925	GUUCCUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICAAUGUG	8325
914	ACAUGGCC A CAGGAACA	926	UGUCCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGCAAUGU	8326
916	AUUGCCAC A GGAACUA	927	UAUGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGGCAU	8327
922	ACAGGAAC A UAUUGUAC	928	GUACAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUCUGU	8328
931	UAUUGUAC A AAAAUCA	929	UGAUUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUACAAU	8329
939	AAAAAUUC A AAUUGUGU	930	ACACAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUUUUU	8330
958	UAGGAAAC U UCCUGUAA	931	UUACAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUUCCUA	8331
961	GAAACUUC C UGUAAACA	932	UGUUUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAGUUUC	8332
962	AAACUUC U GUAAACAG	933	CUGUUUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAAGUUU	8333
969	CUGUAAAC A GGCCUAU	934	AAUAGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUUACAG	8334
973	AAACAGGC C UAUUGAU	935	AAUCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICUGUUU	8335
974	AACAGGCC U AUUGAUUG	936	CAAUCAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGCCUGUU	8336
994	AGUAUGUC A ACGAAUUG	937	CAAUUCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACUAUCU	8337
1009	UGUGGGUC U UUUGGGU	938	ACCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACCCACA	8338
1022	GGGUUUGC C GCCCUCU	939	AAAGGGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICAAACCC	8339
1025	UUUGCCGC C CUUUCAC	940	GUGAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICGGCAA	8340
1026	UUGCCGCC C CUUUCACG	941	CGUGAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGCGGCA	8341
1027	UGCCGCC C UUUCACGC	942	GCGUGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGCGGC	8342
1028	GCCGCC C UUUCACGC	943	UGCGUGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGGCGGC	8343
1032	CCCCUUC A CGCAAUGU	944	ACAUUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAAGGGG	8344
1036	UUUCACGC A AUGUGGAU	945	AUCCACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICGUGAAA	8345
1049	GGAUUAUC U GCUUAAU	946	AUUAAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAUAUCC	8346
1052	UAUUCUGC U UUAUUGCC	947	GGCAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICAGAUUA	8347
1060	UUUAAUGC C UUUAUUG	948	CAUAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICAUUAUA	8348
1061	UUAAUGCC U UUAUUGC	949	GCAUAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGCAUUA	8349
1070	UUUAUUGC A UGCAUACA	950	UGUAUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICAUAUA	8350
1074	AUGCAUGC A UACAAGCA	951	UGCUUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICAUGCAU	8351

1078	AUGCAUAC A AGCAAAAC	952	GUUUUGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUGCAU	8352
1082	AUACAAGC A AAACAGGC	953	GCCUGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUUGUAU	8353
1087	AGCAAAAC A GGCUUUUA	954	UAAAAGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUUGCU	8354
1091	AAACAGGC U UUUACUUU	955	AAAGUAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUGUUU	8355
1097	GUUUUAC U UUCUCGCC	956	GGCGAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAAAAGC	8356
1101	UUACUUUC U CGCCAACU	957	AGUUGGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAGUAA	8357
1105	UUUCUCGC C AACUUACA	958	UGUAAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGAGAA	8358
1106	UUCUCGCC A ACUUACAA	959	UUGUAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAGAGAA	8359
1109	UCGCCAAC U UACAAGGC	960	GCCUUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGGCGA	8360
1113	CAACUUAC A AGGCCUUU	961	AAAGCCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAGUUG	8361
1118	UACAAGGC C UUUCUAG	962	CUUAGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUUGUA	8362
1119	ACAAGGCC U UUCUAGU	963	ACUUAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCUUGU	8363
1123	GGCCUUUC U AAGUAAAC	964	GUUUACUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAGGCC	8364
1132	AAGUAAAC A GUUUGUGA	965	UCACAUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUACUU	8365
1143	AUGUGAAC C UUUACCCC	966	GGGGUAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCACAU	8366
1144	UGUGAAC U UUACCCCG	967	CGGGGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUUCACA	8367
1149	ACUUUAC C CCGUUGCU	968	AGCAACGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAAAGGU	8368
1150	CCUUUACC C CGUUGCUC	969	GAGCAACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUAAAGG	8369
1151	CUUUACCC C GUUGCUCG	970	CGAGCAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGUAAAG	8370
1157	CCCGUUGC U CGGCAACG	971	CGUUGCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAACGGG	8371
1162	UGCUCGGC A ACGCCUG	972	CAGGCCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCGAGCA	8372
1168	GCAACGGC C UGGUCUAU	973	AUAGACCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCGUUGC	8373
1169	CAACGGCC U GGUCUAG	974	CAUAGACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCGUUG	8374
1174	GCCUGGUC U AUGCCAAG	975	CUUGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACCAGGC	8375
1179	GUCUAGC C AAGUGUUU	976	AAACACUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAUAGAC	8376
1180	UCUAGCC A AGUGUUUG	977	CAAACACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAUAGA	8377
1190	GUGUUUGC U GACGCAAC	978	GUUGCGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAACAC	8378
1196	GCUGACGC A ACCCCAC	979	GUGGGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUCAGC	8379
1199	GACGCAAC C CCCACUGG	980	CCAGUGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGCGUC	8380
1200	ACGCAACC C CCACUGGU	981	ACCAGUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUUGCGU	8381
1201	CGCAACCC C CACUGGUU	982	AACCAGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGUUGCG	8382
1202	GCAACCCC C ACUGGUUG	983	CAACCAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGGUUGC	8383
1203	CAACCCCC A CUGGUUGG	984	CCAACCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGGUUG	8384
1205	ACCCCCAC U GGUGGGG	985	CCCCAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGGGGGU	8385
1215	GUUGGGGC U UGGCCAUA	986	UAUGGCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCAAC	8386
1220	GGCUUGGC C AUAGCCA	987	UGGCTUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCAAGCC	8387
1221	GCUUGGCC A UAGGCCAU	988	AUGGCTUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCAAGC	8388
1227	CCAUAGGC C AUCAGCGC	989	GCGCUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCU AUGG	8389
1228	CAUAGGCC A UCAGCGCA	990	UGCGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCU AUG	8390
1231	AGGCCAUC A GCGAUGC	991	GCAUGCGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUGGCCU	8391
1236	AUCAGCGC A UGCGUGGA	992	UCCACGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGUGAU	8392
1247	CGUGGAAC C UUUGUGUC	993	GACACAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCCACG	8393
1248	GUGGAACC U UUGUGUCU	994	AGACACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCCAC	8394
1256	UUUGUGUC U CCUCUGCC	995	GGCAGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACACAAA	8395
1258	UGUGUCUC C UCUGCCGA	996	UCGGCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGACACA	8396
1259	GUGUCUCC U CUGCCGAU	997	AUCGGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGACAC	8397
1261	GUCUCCUC U GCCGAUCC	998	GGAUCGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGAGAC	8398
1264	UCCUCUGC C GAUCCAUA	999	UAUGGAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGAGGA	8399
1269	UGCCGAUC C AUACGCG	1000	CGCGUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUCGGCA	8400
1270	GCCGAUCC A UACCGCG	1001	CCGCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUCGGC	8401
1274	AUCCAUA C GCGAACU	1002	AGUUCGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IU AUGGAU	8402

1282	CGCGGAAC U CCUAGCCG	1003	CGGCUAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCCGCG	8403
1284	CGGAACUC C UAGCCGCU	1004	AGCGGCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUUCCG	8404
1285	GGAAACUCC U AGCCGCUU	1005	AAGCGGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGUUCC	8405
1289	CUCCUAGC C GCUUGUUU	1006	AAACAAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUAGGAG	8406
1292	CUAGCCGC U UGUUUUGC	1007	GCAAAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGCUAG	8407
1301	UGUUUUGC U CGCAGCAG	1008	CUGCUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAAACA	8408
1305	UUGCUCGC A GCAGGUCU	1009	AGACCUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGACAA	8409
1308	CUCGCAGC A GGUCUGGG	1010	CCCAGACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUGCGAG	8410
1313	AGCAGGUC U GGGGCAAA	1011	UUUGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACCUGCU	8411
1319	UCUGGGGC A AAACUCAU	1012	AUGAGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCAGA	8412
1324	GGCAAAAC U CAUCGGGA	1013	UCCCGAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUUGCC	8413
1326	CAAAACUC A UCGGGACU	1014	AGUCCCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUUUUG	8414
1334	AUCGGGAC U GACAAUUC	1015	GAAUUGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCCGAU	8415
1338	GGACUGAC A AUUCUGUC	1016	GACAGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCAGUCC	8416
1343	GACAAUUC U GUCGUGCU	1017	AGCACGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUUGUC	8417
1351	UGUCGUGC U CUCCCGCA	1018	UGC GGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICACGACA	8418
1353	UCGUGCUC U CCCGCAAA	1019	UUUGCGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGCACGA	8419
1355	GUGCUCUC C CGCAAAUA	1020	UAUUUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAGCAC	8420
1356	UGCUCUCC C GCAAAUAU	1021	AUAUUUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGAGCA	8421
1359	UCUCCCGC A AAUAUACA	1022	UGUAUAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGGAGA	8422
1367	AAAUAUAC A UCAUUUCC	1023	GGAAAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUAUUUU	8423
1370	UAUACAUC A UUUCCAUG	1024	CAUGGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUGUAUA	8424
1375	AUCAUUUC C AUGGCUGC	1025	GCAGCCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAUGAU	8425
1376	UCAUUUCC A UGGCUGCU	1026	AGCAGCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAAUGA	8426
1381	UCCAUGGC U GCUAGGCU	1027	AGCCUAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCAUGGA	8427
1384	AUGGCUGC U AGGCUGUG	1028	CACAGCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGCCAU	8428
1389	UGCUAGGC U GUGCUGCC	1029	GGCAGCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUAGCA	8429
1394	GGCUGUGC U GCCAACUG	1030	CAGUUGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICACAGCC	8430
1397	UGUCGUGC C AACUGGAU	1031	AUCCAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGCACA	8431
1398	GUGCUGCC A ACUGGAUC	1032	GAUCCAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCGACAC	8432
1401	CUGCCAAC U GGAUCCUA	1033	UAGGAUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGGCAG	8433
1407	ACUGGAUC C UACGCGGG	1034	CCCGCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUCCAGU	8434
1408	CUGGAUCC U ACGCGGGA	1035	UCCCGCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUCCAG	8435
1421	GGGACGUC C UUGUUUA	1036	UAAACAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACGUCCC	8436
1422	GGACGUCC U UUGUUUAC	1037	GUAAACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGACGUCC	8437
1434	UUUACGUC C CGUCGGCG	1038	CGCCGACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACGUAAA	8438
1435	UUACGUCC C GUCGGCGC	1039	GCGCCGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGACGUAA	8439
1444	GUCGGCGC U GAAUCCCG	1040	CGGGAUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGCCGAC	8440
1450	GCUGAAUC C CGCGGACG	1041	CGUCCGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUCAGC	8441
1451	CUGAAUCC C GCGGACGA	1042	UCGUCCGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUUCAG	8442
1461	CGGACGAC C CCUCCCGG	1043	CCGGGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCGUCCG	8443
1462	GGACGACC C CUCCCGGG	1044	CCCGGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCGUCC	8444
1463	GACGACCC C UCCCGGGG	1045	CCCCGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGUCGUC	8445
1464	ACGACCCC U CCCGGGGC	1046	GCCCCGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGGUCGU	8446
1466	GACCCUC C CGGGGCCG	1047	CGGCCCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGGGUC	8447
1467	ACCCUCC C GGGGCCGC	1048	GCGGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGGGGU	8448
1473	CCCGGGGC C GCUUGGGG	1049	CCCCAAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCGGG	8449
1476	GGGGCCGC U UGGGGCUC	1050	GAGCCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGCCCC	8450
1483	CUUGGGGC U CUACCGCC	1051	GGCGGUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCAAG	8451
1485	UGGGGCUC U ACCGCCCG	1052	CGGGCGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGCCCCA	8452
1488	GGCUCUAC C GCCCGCUU	1053	AAGCGGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAGAGCC	8453

1491	UCUACCGC C CGCUUCUC	1054	GAGAAGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGUAGA	8454
1492	CUACCGCC C GCUUCUCC	1055	GGAGAAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGUAG	8455
1495	CCGCCCGC U UCUCGCC	1056	GGCGGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGGCGG	8456
1498	CCCGCUUC U CCGCCUUA	1057	AUAGGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGCGGG	8457
1500	CGCUUCUC C GCCUAUUG	1058	CAAUAGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAAGCG	8458
1503	UUCUCCGC C UAUUGUAC	1059	GUACAAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGAGAA	8459
1504	UCUCCGCC U AUUGUACC	1060	GGUACAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGAGAA	8460
1512	UAUUGUAC C GACCGUCC	1061	GGACGGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUACAAUA	8461
1516	GUACCGAC C GUCCACGG	1062	CCGUGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCGGUAC	8462
1520	CGACCGUC C ACGGGGCG	1063	CGCCCCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACGGUCG	8463
1521	GACCGUCC A CGGGGCGC	1064	GCGCCCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGACGGUC	8464
1530	CGGGGCGC A CCUCUCU	1065	AAGAGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGCCCCG	8465
1532	GGGCGCAC C UCUCUUUA	1066	UAAAGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCGCCC	8466
1533	GGCGCACC U CUCUUUAC	1067	GUAAAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGCGCC	8467
1535	CGCACCUC U CUUUACGC	1068	GCGUAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGUGCG	8468
1537	CACCUCUC U UUACGCGG	1069	CCGCGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAGGUG	8469
1548	ACGCGGAC U CCCCGUCU	1070	AGACGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCGCGU	8470
1550	GCGGACUC C CCGUCUGU	1071	ACAGACGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUCCGC	8471
1551	CGGACUCC C CGUCUGUG	1072	CACAGACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGUCCG	8472
1552	GGACUCCC C GUCUGUGC	1073	GCACAGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGAGUCC	8473
1556	UCCCCGUC U GUGCCUUC	1074	GAAGGCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACGGGGA	8474
1561	GUCUGUGC C UUCUCAUC	1075	GAUGAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICACAGAC	8475
1562	UCUGUGCC U UCUCAUCU	1076	AGAUGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCACAGA	8476
1565	GUGCCUUC U CAUCUGCC	1077	GGCAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGGCAC	8477
1567	GCCUUCUC A UCUGCCGG	1078	CCGGCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAAGGC	8478
1570	UUCUCAUC U GCCGGACC	1079	GGUCCGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUGAGAA	8479
1573	UCAUCUGC C GGACCGUG	1080	CACGGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGAUGA	8480
1578	UGCCGGAC C GUGUGCAC	1081	GUGCACAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCGGCA	8481
1585	CCGUGUGC A CUUCGCUU	1082	AAGCGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICACACGG	8482
1587	GUGUGCAC U UCGCUUCA	1083	UGAAGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCACAC	8483
1592	CACUUCGC U UCACUCU	1084	AGAGGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGAAGUG	8484
1595	UUCGCUUC A CCUCUGCA	1085	UGCAGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGCGAA	8485
1597	CGCUUCAC C UCUGCACG	1086	CGUGCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAAGCG	8486
1598	GCUUCACC U CUGCACGU	1087	ACGUGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGAAGC	8487
1600	UUCACCUC U GCACGUCG	1088	CGACGUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGUGAA	8488
1603	ACCUCUGC A CGUCGCAU	1089	AUGCGACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGAGGU	8489
1610	CACGUCGC A UGGAGACC	1090	GGUCUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGACGUG	8490
1618	AUGGAGAC C ACCGUGAA	1091	UUCACGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCUCCAU	8491
1619	UGGAGACC A CCGUGAAC	1092	GUUCACGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCUCCA	8492
1621	GAGACCAC C GUGAACGC	1093	GCGUUCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGGUCUC	8493
1630	GUGAACGC C CACAGGAA	1094	UUCUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGUUCAC	8494
1631	UGAACGCC C ACAGGAAC	1095	GUUCUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGUUCA	8495
1632	GAACGCC C CAGGAACC	1096	GGUUCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGCGUUC	8496
1634	ACGCCAC A GGAACUG	1097	CAGGUUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGGGCGU	8497
1640	ACAGGAAC C UGCCAAG	1098	CUUGGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCCUGU	8498
1641	CAGGAACC U GCCCAAGG	1099	CCUUGGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUUCCUG	8499
1644	GAACUGGC C CAAGGUCU	1100	AGACCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGUUC	8500
1645	AACUGGCC C AAGGUCU	1101	AAGACCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAGGUU	8501
1646	ACCUGCCC A AGGUCUUG	1102	CAAGACCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGCAGGU	8502
1652	CCAAGGUC U UGCAUAG	1103	CUUAUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACCUUGG	8503
1656	GGUCUUGC A UAAGAGGA	1104	UCCUCUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAGACC	8504

1666	AAGAGGAC U CUUGGACU	1105	AGUCCAAG CUGAUGAG	GCCGUUAGGC	CGAA IUCCUCUU	8505
1668	GAGGACUC U UGGACUUU	1106	AAAGUCCA CUGAUGAG	GCCGUUAGGC	CGAA IAGUCCUC	8506
1674	UCUUGGAC U UUCAGCAA	1107	UUGCUGAA CUGAUGAG	GCCGUUAGGC	CGAA IUCCAAGA	8507
1678	GGACUUUC A GCAAUGUC	1108	GACAUUGC CUGAUGAG	GCCGUUAGGC	CGAA IAAAGUCC	8508
1681	CUUUCAGC A AUGUCAAC	1109	GUUGACAU CUGAUGAG	GCCGUUAGGC	CGAA ICUGAAAG	8509
1687	GCAAUGUC A ACGACCGA	1110	UCGGUCGU CUGAUGAG	GCCGUUAGGC	CGAA IACAUUGC	8510
1693	UCAACGAC C GACCUUGA	1111	UCAAGGUC CUGAUGAG	GCCGUUAGGC	CGAA IUCGUUGA	8511
1697	CGACCGAC C UUGAGGCA	1112	UGCCUCAA CUGAUGAG	GCCGUUAGGC	CGAA IUCGGUCG	8512
1698	GACCGACC U UGAGGCAU	1113	AUGCCUCA CUGAUGAG	GCCGUUAGGC	CGAA IGUCGGUC	8513
1705	CUUGAGGC A UACUUCAA	1114	UUGAAGUA CUGAUGAG	GCCGUUAGGC	CGAA ICCUCAAG	8514
1709	AGGCAUAC U UCAAAGAC	1115	GUCUUUGA CUGAUGAG	GCCGUUAGGC	CGAA IUAUGCCU	8515
1712	CAUACUUC A AAGACUGU	1116	ACAGUCUU CUGAUGAG	GCCGUUAGGC	CGAA IAAGUAUG	8516
1718	UCAAAGAC U GUGUGUUU	1117	AAACACAC CUGAUGAG	GCCGUUAGGC	CGAA IUCUUUGA	8517
1769	UAAAGGUC U UUGUACUA	1118	UAGUACAA CUGAUGAG	GCCGUUAGGC	CGAA IACCUUUA	8518
1776	CUUUGUAC U AGGAGGCU	1119	AGCCUCCU CUGAUGAG	GCCGUUAGGC	CGAA IUACAAAG	8519
1784	UAGGAGGC U GUAGGCAU	1120	AUGCCUAC CUGAUGAG	GCCGUUAGGC	CGAA ICCUCCUA	8520
1791	CUGUAGGC A UAAAUUGG	1121	CCAUUUUA CUGAUGAG	GCCGUUAGGC	CGAA ICCUACAG	8521
1807	GUGUGUUC A CCAGCACC	1122	GGUGCUGG CUGAUGAG	GCCGUUAGGC	CGAA IAACACAC	8522
1809	GUGUUCAC C AGCACCAU	1123	AUGGUGCU CUGAUGAG	GCCGUUAGGC	CGAA IUGAACAC	8523
1810	UGUUCACC A GCACCAUG	1124	CAUGGUGC CUGAUGAG	GCCGUUAGGC	CGAA IGUGAACAC	8524
1813	UCACCAGC A CCAUGCAA	1125	UUGCAUGG CUGAUGAG	GCCGUUAGGC	CGAA ICUGGUGA	8525
1815	ACCAGCAC C AUGCAACU	1126	AGUUGCAU CUGAUGAG	GCCGUUAGGC	CGAA IUGCUGGU	8526
1816	CCAGCACC A UGCAACUU	1127	AAGUUGCA CUGAUGAG	GCCGUUAGGC	CGAA IGUGCUGG	8527
1820	CACCAUGC A ACUUUUUC	1128	GAAAAAGU CUGAUGAG	GCCGUUAGGC	CGAA ICAUGGUG	8528
1823	CAUGCAAC U UUUUCACC	1129	GGUGAAAA CUGAUGAG	GCCGUUAGGC	CGAA IUUGCAUG	8529
1829	ACUUUUUC A CCUCUGCC	1130	GGCAGAGG CUGAUGAG	GCCGUUAGGC	CGAA IAAAAAGU	8530
1831	UUUUUCAC C UCUGCCUA	1131	UAGGCAGA CUGAUGAG	GCCGUUAGGC	CGAA IUGAAAAA	8531
1832	UUUUCACC U CUGCCUAA	1132	UUAGGCAG CUGAUGAG	GCCGUUAGGC	CGAA IGUGAAAA	8532
1834	UUCACCUC U GCCUAAUC	1133	GAUUAGGC CUGAUGAG	GCCGUUAGGC	CGAA IAGGUGAA	8533
1837	ACCUCUGC C UAAUCAUC	1134	GAUGAUUA CUGAUGAG	GCCGUUAGGC	CGAA ICAGAGGU	8534
1838	CCUCUGCC U AAUCAUCU	1135	AGAUGAUU CUGAUGAG	GCCGUUAGGC	CGAA IGCAGAGG	8535
1843	GCCUAAUC A UCUCAUGU	1136	ACAUGAGA CUGAUGAG	GCCGUUAGGC	CGAA IAUUAGGC	8536
1846	UAAUCAUC U CAUGUUCA	1137	UGAACAUU CUGAUGAG	GCCGUUAGGC	CGAA IAUGAUUA	8537
1848	AUCAUCUC A UGUUCAUG	1138	CAUGAACA CUGAUGAG	GCCGUUAGGC	CGAA IAGAUGAU	8538
1854	UCAUGUUC A UGUCCUAC	1139	GUAGGACA CUGAUGAG	GCCGUUAGGC	CGAA IAACAUGA	8539
1859	UUAUGUC C UACUGUUC	1140	GAACAGUA CUGAUGAG	GCCGUUAGGC	CGAA IACAUGAA	8540
1860	UCAUGUCC U ACUGUUCA	1141	UGAACAGU CUGAUGAG	GCCGUUAGGC	CGAA IGACAUGA	8541
1863	UGUCCUAC U GUUCAAGC	1142	GCUUGAAC CUGAUGAG	GCCGUUAGGC	CGAA IUAGGACA	8542
1868	UACUGUUC A AGCCUCCA	1143	UGGAGGCU CUGAUGAG	GCCGUUAGGC	CGAA IAACAGUA	8543
1872	GUUCAAGC C UCCAAGCU	1144	AGCUUGGA CUGAUGAG	GCCGUUAGGC	CGAA ICUUGAAC	8544
1873	UUCAAGCC U CCAAGCUG	1145	CAGCUUGG CUGAUGAG	GCCGUUAGGC	CGAA IGCUUGAA	8545
1875	CAAGCCUC C AAGCUGUG	1146	CACAGCUU CUGAUGAG	GCCGUUAGGC	CGAA IAGGCUUG	8546
1876	AAGCCUCC A AGCUGUGC	1147	GCACAGCU CUGAUGAG	GCCGUUAGGC	CGAA IGAGGCUU	8547
1880	CUCCAAGC U GUGCCUUG	1148	CAAGGCAC CUGAUGAG	GCCGUUAGGC	CGAA ICUUGGAG	8548
1885	AGCUGUGC C UUGGGUGG	1149	CCACCCAA CUGAUGAG	GCCGUUAGGC	CGAA ICACAGCU	8549
1886	GCUGUGCC U UGGGUGGC	1150	GCCACCCA CUGAUGAG	GCCGUUAGGC	CGAA IGCACAGC	8550
1895	UGGGUGGC U UUGGGGCA	1151	UGCCCCAA CUGAUGAG	GCCGUUAGGC	CGAA ICCACCCA	8551
1903	UUUGGGGC A UGGACAUU	1152	AAUGUCCA CUGAUGAG	GCCGUUAGGC	CGAA ICCCCAAA	8552
1909	GCAUGGAC A UUGACCCG	1153	CGGGUCAA CUGAUGAG	GCCGUUAGGC	CGAA IUCCAUGC	8553
1915	ACAUGUAC C CGUAUAAA	1154	UUUAUACG CUGAUGAG	GCCGUUAGGC	CGAA IUCAAUGU	8554
1916	CAUUGACC C GUAAUAAAG	1155	CUUUAUAC CUGAUGAG	GCCGUUAGGC	CGAA IGUCAAUG	8555

1935	UUUGGAGC U UCUGUGGA	1156	UCCACAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUCCAAA	8556
1938	GGAGCUC U GUGGAGUU	1157	AACUCCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGCUCC	8557
1949	GGAGUUAC U CUCUUUUU	1158	AAAAAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAAACUCC	8558
1951	AGUUACUC U CUUUUUUG	1159	CAAAAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUAAACU	8559
1953	UUACUCUC U UUUUUGCC	1160	GGCAAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAGUAA	8560
1961	UUUUUUGC C UUCUGACU	1161	AGUCAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAAAAA	8561
1962	UUUUUGCC U UCUGACUU	1162	AAGUCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAAAAA	8562
1965	UUGCCUUC U GACUUCUU	1163	AAGAAGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGGCAG	8563
1969	CUUCUGAC U UCUUUCCU	1164	AGGAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCAGAAG	8564
1972	CUGACUUC U UUCUUCU	1165	AGAAGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGUCAG	8565
1976	CUUCUUUC C UUCUAUUC	1166	GAAUAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAGAAG	8566
1977	UUCUUUCC U UCUAUUCG	1167	CGAAUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAAGAA	8567
1980	UUUCCUUC U AUUCGAGA	1168	UCUCGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGGAAA	8568
1991	UCGAGAUC U CCUCGACA	1169	UGUCGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUCUCGA	8569
1993	GAGAUCUC C UCGACACC	1170	GGUGUCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAUCUC	8570
1994	AGAUCUCC U CGACACCG	1171	CGGUGUCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGAUCU	8571
1999	UCCUCGAC A CCGCCUCU	1172	AGAGGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCGAGGA	8572
2001	CUCGACAC C GCCUCUGC	1173	GCAGAGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGUCGAG	8573
2004	GACACCGC C UCUGCUCU	1174	AGAGCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGUGUC	8574
2005	ACACCGCC U CUGCUCUG	1175	CAGAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGUGU	8575
2007	ACCGCCUC U GCUCUGUA	1176	UACAGAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGCGGU	8576
2010	GCCUCUGC U CUGUAUCG	1177	CGAUACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGAGGC	8577
2012	CUCUGCUC U GUUACGGG	1178	CCCGAUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGCAGAG	8578
2025	CGGGGGGC C UUAGAGUC	1179	GACUCUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCCCG	8579
2026	GGGGGGCC U UAGAGUCU	1180	AGACUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCCCCC	8580
2034	UUAGAGUC U CCGGAACA	1181	UGUUCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACUCUAA	8581
2036	AGAGUCUC C GGAACAUU	1182	AAUGUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGACUCU	8582
2042	UCCGGAAC A UUGUUCAC	1183	GUGAACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCCGGA	8583
2049	CAUUGUUC A CCUCACCA	1184	UGGUGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAACAAUG	8584
2051	UUGUUCAC C UCACCAUA	1185	UAUGGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAACAA	8585
2052	UGUUCACC U CACCAUAC	1186	GUAUGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGAACAA	8586
2054	UUCACCUC A CCAUACGG	1187	CCGUUAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGUGAA	8587
2056	CACCUCAC C AUACGGCA	1188	UGCCGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAGGGUG	8588
2057	ACCUCACC A UACGGCAC	1189	GUGCCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGAGGU	8589
2064	CAUACGGC A CUCAGGCA	1190	UGCCUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCGUUAG	8590
2066	UACGGCAC U CAGGCAAG	1191	CUUGCCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCCGUA	8591
2068	CGGCACUC A GGCAAGCU	1192	AGCUUGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUGCCG	8592
2072	ACUCAGGC A AGCUAUUC	1193	GAAUAGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUGAGU	8593
2076	AGGCAAGC U AUUCUGUG	1194	CACAGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUUGCCU	8594
2081	AGCUAUUC U GUGUUGGG	1195	CCCAACAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUAGCU	8595
2105	GAUGAAUC U AGCCACCU	1196	AGGUGGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUCAUC	8596
2109	AAUCUAGC C ACCUGGGU	1197	ACCCAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUGAAUU	8597
2110	AUCUAGCC A CCUGGGUG	1198	CACCCAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCUGAGU	8598
2112	CUAGCCAC C UGGGUGGG	1199	CCCACCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGGCUAG	8599
2113	UAGCCACC U GGGUGGGA	1200	UCCCACCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGGCUA	8600
2138	GGAAGAUC C AGCAUCCA	1201	UGGAUGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUCUUCC	8601
2139	GAAGAUC A GCAUCCAG	1202	CUGGAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUCUUC	8602
2142	GAUCCAGC A UCCAGGGA	1203	UCCUGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUGGAUC	8603
2145	CCAGCAUC C AGGGAAUU	1204	AAUUCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUCUGG	8604
2146	CAGCAUCC A GGGAUUUA	1205	UAAUUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUCUG	8605
2161	UAGUAGUC A GCUAUGUC	1206	GACAUAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACUACUA	8606

2164	UAGUCAGC U AUGUCAAC	1207	GUUGACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUGACUA	8607
2170	GCUAUGUC A ACGUUAU	1208	AUUAACGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACAUAGC	8608
2185	AUAUGGGC C UAAAAAUC	1209	GAUUUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCAUUA	8609
2186	UAUGGGCC U AAAAAUCA	1210	UGAUUUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCCAUA	8610
2194	UAAAAAUC A GACAACUA	1211	UAGUUGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUUUUA	8611
2198	AAUCAGAC A ACUAUUGU	1212	ACAAUAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCUGAUU	8612
2201	CAGACAAC U AUUGUGGU	1213	ACCACAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGUCUG	8613
2213	GUGGUUUC A CAUUCUUC	1214	AGGAAAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAACCAC	8614
2215	GGUUUCAC A UUUCUUGU	1215	ACAGGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAAACC	8615
2220	CACAUUUC C UGUCUUAU	1216	GUAAGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAUGUG	8616
2221	ACAUUUCU U GUCUUAU	1217	AGUAAGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAUGU	8617
2225	UUCUGUC U UACUUUUG	1218	CAAAAGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACAGGAA	8618
2229	UGUCUUAU U UUUGGGCG	1219	CGCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAAGACA	8619
2244	CGAGAAAC U GUUCUUGA	1220	UCAAGAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUCUCG	8620
2249	AACUGUUC U UGAAUAUU	1221	AAUAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAACAGUU	8621
2265	UUGGUGUC U UUUGGAGU	1222	ACUCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACACCAA	8622
2284	GGAUUCGC A CUCCUCCU	1223	AGGAGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGAAUCC	8623
2286	AUUCGCAC U CCUCUUGC	1224	GCAGGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCGAAU	8624
2288	UCGCACUC C UCCUGCAU	1225	AUGCAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUGCGA	8625
2289	CGCACUCC U CCUGCAUA	1226	UAUGCAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGUGCG	8626
2291	CACUCCUC C UGCAUAUA	1227	UAUAUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGAGUG	8627
2292	ACUCCUCC U GCAUAUAG	1228	CUAUAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGGAGU	8628
2295	CCUCCUGC A UAUAGACC	1229	GGUCUAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGAGG	8629
2303	AUAUAGAC C ACCAAAUG	1230	CAUUUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCUAUAU	8630
2304	UAUAGACC A CCAAUGC	1231	GCAUUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCUAUA	8631
2306	UAGACCAC C AAAUGCCC	1232	GGGCAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGGUCUA	8632
2307	AGACCACC A AAUGCCCC	1233	GGGGCAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGGUCU	8633
2313	CCAAUGC C CCUAUCUU	1234	AAGAUAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAUUUGG	8634
2314	CAAUGCC C CUAUCUUA	1235	UAAGAUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAUUUG	8635
2315	AAAUGCCC C UAUCUUAU	1236	AUAAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGCAUUU	8636
2316	AAUGCCCC U AUCUUAUC	1237	GAUAAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGGCAUU	8637
2320	CCCCUUAU C UAUCAACA	1238	UGUUGAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUAGGGG	8638
2325	AUCUUAUC A ACACUCC	1239	GGAAGUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUAGAU	8639
2328	UUAUCAAC A CUUCCGGA	1240	UCCGGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGAUAA	8640
2330	AUCAACAC U UCCGGAUA	1241	UUUCCGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGUUGAU	8641
2333	AACACUUC C GGAAACUA	1242	UAGUUUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGUGUU	8642
2340	CCGGAAC U ACUGUUGU	1243	ACAACAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCCGG	8643
2343	GAAACUAC U GUUGUUG	1244	CUAACAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAGUUUC	8644
2362	GAAGAGGC A GGUCCCCU	1245	AGGGGACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUCUUC	8645
2367	GGCAGGUC C CCUAGAAG	1246	CUUCUAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACCUGCC	8646
2368	GCAGGUCC C CUAGAAGA	1247	UCUUCUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGACCUGC	8647
2369	CAGGUCCC C UAGAAGAA	1248	UUCUUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGACCUG	8648
2370	AGGUCCCC U AGAAGAAG	1249	CUUCUUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGACCU	8649
2382	AGAAGAAC U CCCUCGCC	1250	GGCGAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCUUCU	8650
2384	AAGAACUC C CUCGCCUC	1251	GAGGCGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUUCUU	8651
2385	AGAACUCC C UCGCCUCG	1252	CGAGGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUUCU	8652
2386	GAACUCCC U CGCCUCGC	1253	GCGAGGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGAGUUC	8653
2390	UCCUCUGC C UCGCAGAC	1254	GUCUGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGGGA	8654
2391	CCCUCGCC U CGCAGACG	1255	CGUCUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGAGGGG	8655
2395	CGCCUCGC A GACGAAGG	1256	CCUUCGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGAGGCG	8656
2406	CGAAGGUC U CAAUCGCC	1257	GGCGAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACCUUCG	8657

2408	AAGGUCUC A AUCGCCGC	1258	GCGGCGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGACCUU	8658
2414	UCAAUCGC C GCGUCGCA	1259	UGCGACGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGAUUGA	8659
2422	CGCGUCGC A GAAGAUCU	1260	AGAUCUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGACGCG	8660
2430	AGAAGAUC U CAAUCUCG	1261	CGAGAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUCUUCU	8661
2432	AAGAUCUC A AUCUCGGG	1262	CCCGAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAUCUU	8662
2436	UCUCAAUC U CGGGAAUC	1263	GAUUCCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUGAGAG	8663
2445	CGGGAAUC U CAAUGUUA	1264	UAACAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUCCCG	8664
2447	GGAAUCUC A AUGUUGU	1265	ACUAACAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAUCUCC	8665
2460	UAGUAUUC C UUGGACAC	1266	GUGUCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUACUA	8666
2461	AGUAUUC U UGGACACA	1267	UGUGUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAUACU	8667
2467	CCUUGGAC A CAUAAGGU	1268	ACCUUAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCAAGG	8668
2469	UUGGACAC A UAAGGUGG	1269	CCACCUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGUCCAA	8669
2483	UGGGAAAC U UACGGGG	1270	CCCCGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCCCA	8670
2493	UACGGGGC U UUAUUCU	1271	AAGAAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCGUA	8671
2500	CUUUAUUC U UCUACGGU	1272	ACCGUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUAAAG	8672
2503	UAUUCUUC U ACGGUACC	1273	GGUACCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGAAUA	8673
2511	UACGGUAC C UUGCUUUA	1274	UAAAGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUACCGUA	8674
2512	ACGGUACC U UGCUUUA	1275	UUAAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUACCGU	8675
2516	UACCUUGC U UUAUCCU	1276	AGGAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAGGUA	8676
2523	CUUUAUC C UAAUAGGC	1277	GCCAUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUAUAAAG	8677
2524	UUUAUCC U AAUAGGCA	1278	UGCCAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUUAUA	8678
2532	UAAUAGGC A AACUCCU	1279	AAGGAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCAUUUA	8679
2536	UGGCAAAC U CCUUCUU	1280	AAAGAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUGCCA	8680
2538	GCAAACUC C UUCUUUUC	1281	GAAAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUUUGC	8681
2539	CAAACUCC U UCUUUUCC	1282	GGAAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGUUUG	8682
2542	ACUCCUUC U UUCCUGA	1283	UCAGGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGGAGU	8683
2547	UUCUUUUC C UGACAUUC	1284	GAAUGUCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAAGAA	8684
2548	UCUUUUC C UGACAUUC	1285	UGAAUGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAAAGA	8685
2552	UUCUGAC A UUCAUUUG	1286	CAAUGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCAGGAA	8686
2556	UGACAUUC A UUUGCAGG	1287	CCUGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUGUCA	8687
2562	UCAUUUGC A GGAGACA	1288	UGUCCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAUGA	8688
2570	AGGAGGAC A UUGUUGAU	1289	AUCAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCUCCU	8689
2589	AUGUAAGC A AUUUGUGG	1290	CCACAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUUACAU	8690
2601	UGUGGGGC C CUUACAG	1291	CUGUAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCACA	8691
2602	GUGGGGCC C CUUACAGU	1292	ACUGUAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCCCAC	8692
2603	UGGGGGCC C UUACAGUA	1293	UACUGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGCCCCA	8693
2604	GGGGCCCC U UACAGUAA	1294	UUACUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGCCCC	8694
2608	CCCCUAC A GUAAUGA	1295	UCAUUUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAGGGG	8695
2621	AUGAAAAC A GGAGACUU	1296	AAGUCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUUCAU	8696
2628	CAGGAGAC U UAAAUUA	1297	UUAUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCUCCUG	8697
2638	AAAUUAAC U AUGCCUGC	1298	GCAGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUAUUU	8698
2643	AACUAUGC C UGCUAGGU	1299	ACCUAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAUAGUU	8699
2644	ACUAUGCC U GCUAGGUU	1300	AACCUAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAUAGU	8700
2647	AUGCCUGC U AGGUUUUA	1301	UAAACCUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGCAU	8701
2658	GUUUUAUC C CAUGUUA	1302	UAACAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUAAAAC	8702
2659	UUUAUCC C AAUGUAC	1303	GUAACAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUAAAA	8703
2660	UUUAUCC A AUGUUAU	1304	AGUAACAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUAAA	8704
2668	AAUGUUAUC U AAUAUUU	1305	AAUAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUACAUCU	8705
2679	AUAUUUGC C CUUAGUA	1306	UAUCUAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAAUUA	8706
2680	UAUUUGCC C UUAUAUA	1307	UUAUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAAAUA	8707
2681	AUUUGCCC U UAGAUAAA	1308	UUUAUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGCAAAU	8708

2696	AAGGGAUC A AACCGUAA	1309	AUACGGUU CUGAUGAG	GCCGUUAGGC	CGAA	IAUCCCUU	8709
2700	GAUCAAAC C GUUUUAUC	1310	GAUAAUAC CUGAUGAG	GCCGUUAGGC	CGAA	IUUUGAUC	8710
2709	GUUUUAUC C AGAGUAUG	1311	CAUACUCU CUGAUGAG	GCCGUUAGGC	CGAA	IAUAAUAC	8711
2710	UAUUUAUC A GAGUAUGU	1312	ACAUACUC CUGAUGAG	GCCGUUAGGC	CGAA	IGAUAUAU	8712
2727	AGUUAAUC A UUAUUUCC	1313	GGAAGUAA CUGAUGAG	GCCGUUAGGC	CGAA	IAUUAACU	8713
2732	AUCAUUAC U UCCAGACG	1314	CGUCUGGA CUGAUGAG	GCCGUUAGGC	CGAA	IUAUUGAU	8714
2735	AUUACUUC C AGACGCGA	1315	UCGCGUCU CUGAUGAG	GCCGUUAGGC	CGAA	IAAGUAAU	8715
2736	UUACUUCC A GACGCGAC	1316	GUCGCGUC CUGAUGAG	GCCGUUAGGC	CGAA	IGAAGUAA	8716
2745	GACGCGAC A UUAUUUAC	1317	GUAAAUAA CUGAUGAG	GCCGUUAGGC	CGAA	IUCGCGUC	8717
2754	UUUUUUAC A CACUCUUU	1318	AAAGAGUG CUGAUGAG	GCCGUUAGGC	CGAA	IUAAAUAA	8718
2756	AUUUACAC A CUCUUUGG	1319	CCAAAGAG CUGAUGAG	GCCGUUAGGC	CGAA	IUGUAAAU	8719
2758	UUACACAC U CUUUGGAA	1320	UUCCAAAG CUGAUGAG	GCCGUUAGGC	CGAA	IUGUGUAA	8720
2760	ACACACUC U UUGGAAGG	1321	CCUUCCAA CUGAUGAG	GCCGUUAGGC	CGAA	IAGUGUGU	8721
2777	CGGGGAUC U UAUUAAAA	1322	UUUUAUUA CUGAUGAG	GCCGUUAGGC	CGAA	IAUCCCCG	8722
2794	AGAGAGUC C ACACGUAG	1323	CUACGUGU CUGAUGAG	GCCGUUAGGC	CGAA	IACUCUCU	8723
2795	GAGAGUCC A CACGUAGC	1324	GCUACGUG CUGAUGAG	GCCGUUAGGC	CGAA	IGACUCUC	8724
2797	GAGUCCAC A CGUAGCGC	1325	GCGCUACG CUGAUGAG	GCCGUUAGGC	CGAA	IUGGACUC	8725
2806	CGUAGCGC C UCAUUUUG	1326	CAAAAUGA CUGAUGAG	GCCGUUAGGC	CGAA	ICGCUACG	8726
2807	GUAGCGCC U CAUUUUGC	1327	GCAAAAUG CUGAUGAG	GCCGUUAGGC	CGAA	IGCGCUAC	8727
2809	AGCGCCUC A UUUUGCGG	1328	CCGCAAAA CUGAUGAG	GCCGUUAGGC	CGAA	IAGGCGCU	8728
2821	UGCGGGUC A CCAUAUUC	1329	GAAUAUGG CUGAUGAG	GCCGUUAGGC	CGAA	IACCCGCA	8729
2823	CGGGUCAC C AUAUUUCU	1330	AAGAAUUA CUGAUGAG	GCCGUUAGGC	CGAA	IUGACCCG	8730
2824	GGGUCACC A UAUCUUG	1331	CAAGAAUA CUGAUGAG	GCCGUUAGGC	CGAA	IGUACCCC	8731
2830	CCAUAUUC U UGGGAACA	1332	UGUUCCCA CUGAUGAG	GCCGUUAGGC	CGAA	IAUAUUGG	8732
2838	UUGGGAAC A AGAUCUAC	1333	GUAGAUCU CUGAUGAG	GCCGUUAGGC	CGAA	IUUCCCAA	8733
2844	ACAAGAUC U ACAGCAUG	1334	CAUGCUGU CUGAUGAG	GCCGUUAGGC	CGAA	IAUCUUGU	8734
2847	AGAUCUAC A GCAUGGGA	1335	UCCCAUGC CUGAUGAG	GCCGUUAGGC	CGAA	IUAGAUCU	8735
2850	UCUACAGC A UGGGAGGU	1336	ACCUCCCA CUGAUGAG	GCCGUUAGGC	CGAA	ICUGUAGA	8736
2864	GGUUGGUC U UCCAAACC	1337	GGUUUGGA CUGAUGAG	GCCGUUAGGC	CGAA	IACCAACC	8737
2867	UGGUCUUC C AAACCUCG	1338	CGAGGUUU CUGAUGAG	GCCGUUAGGC	CGAA	IAAGACCA	8738
2868	GGUCUUC C AACCUCGA	1339	UCGAGGUU CUGAUGAG	GCCGUUAGGC	CGAA	IGAAGACC	8739
2872	UCCAAAC C UCGAAAAG	1340	CUUUUCGA CUGAUGAG	GCCGUUAGGC	CGAA	IUUUGGAA	8740
2873	UCCAAACC U CGAAAAGG	1341	CCUUUUCG CUGAUGAG	GCCGUUAGGC	CGAA	IGUUUGGA	8741
2883	GAAAAGGC A UGGGACA	1342	UGUCCCCA CUGAUGAG	GCCGUUAGGC	CGAA	ICCUUUUC	8742
2891	AUGGGGAC A AAUCUUUC	1343	GAAAGAUU CUGAUGAG	GCCGUUAGGC	CGAA	IUCCCCAU	8743
2896	GACAAUUC U UUCUGUCC	1344	GGACAGAA CUGAUGAG	GCCGUUAGGC	CGAA	IAUUUGUC	8744
2900	AAUCUUUC U GUCCCCAA	1345	UUGGGGAC CUGAUGAG	GCCGUUAGGC	CGAA	IAAAGAUU	8745
2904	UUUCUGUC C CCAUCCCC	1346	GGGAUUGG CUGAUGAG	GCCGUUAGGC	CGAA	IACAGAAA	8746
2905	UUCUGUCC C CAUCCCC	1347	GGGGAUUG CUGAUGAG	GCCGUUAGGC	CGAA	IGACAGAA	8747
2906	UCUGUCCC C AAUCCCCU	1348	AGGGGAUU CUGAUGAG	GCCGUUAGGC	CGAA	IGGACAGA	8748
2907	CUGUCCCC A AUCCCCUG	1349	CAGGGGAU CUGAUGAG	GCCGUUAGGC	CGAA	IGGGACAG	8749
2911	CCCCAAUC C CUUGGGAU	1350	AUCCAGG CUGAUGAG	GCCGUUAGGC	CGAA	IAUUGGGG	8750
2912	CCCAAUCC C CUGGGAUU	1351	AAUCCAG CUGAUGAG	GCCGUUAGGC	CGAA	IGAUGGGG	8751
2913	CCAAUCCC C UGGGAUUC	1352	GAAUCCA CUGAUGAG	GCCGUUAGGC	CGAA	IGGAUUGG	8752
2914	CAAUCCCC U GGGAUUCU	1353	AGAAUCCC CUGAUGAG	GCCGUUAGGC	CGAA	IGGGAUUG	8753
2922	UGGGAUUC U UCCCCGAU	1354	AUCGGGGA CUGAUGAG	GCCGUUAGGC	CGAA	IAAUCCCA	8754
2925	GAUUCUUC C CCGAUCAU	1355	AUGAUCGG CUGAUGAG	GCCGUUAGGC	CGAA	IAAGAAUC	8755
2926	AUUCUUC C CGAUCAUC	1356	GAUGAUCG CUGAUGAG	GCCGUUAGGC	CGAA	IGAAGAAU	8756
2927	UUCUUC C GAUCAUCA	1357	UGAUGAUC CUGAUGAG	GCCGUUAGGC	CGAA	IGGAAGAA	8757
2932	CCCCGAUC A UCAGUUGG	1358	CCAACUGA CUGAUGAG	GCCGUUAGGC	CGAA	IAUCGGGG	8758
2935	CGAUCAUC A GUUGGACC	1359	GGUCCAAC CUGAUGAG	GCCGUUAGGC	CGAA	IAUGAUCG	8759

2943	AGUUGGAC C CUGCAUUC	1360	GAAUGCAG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUCCAACU	8760
2944	GUUGGACC C UGCAUUCA	1361	UGAAUGCA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGUCCAAC	8761
2945	UUGGACCC U GCAUUCAA	1362	UUGAAUGC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGUCCAA	8762
2948	GACCCUGC A UUCAAGC	1363	GCUUUGAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICAGGGUC	8763
2952	CUGCAUUC A AAGCCAAC	1364	GUUGGCUU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAAUGCAG	8764
2957	UUCAAGC C AACUCAGU	1365	ACUGAGUU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICUUUGAA	8765
2958	UCAAGACC A ACUCAGUA	1366	UACUGAGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCUUUGA	8766
2961	AAGCCAAC U CAGUAAAU	1367	AUUUACUG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUGGCUU	8767
2963	GCCAACUC A GUAAAUCC	1368	GGAUUUAC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAGUUGGC	8768
2971	AGUAAUUC C AGAUUGGG	1369	CCCAAUCU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAUUUACU	8769
2972	GUAAAUCC A GAUUGGGA	1370	UCCCAAUC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGAUUUAC	8770
2982	AUUGGGAC C UCAACCCG	1371	CGGGUUGA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUCCCAAU	8771
2983	UUGGGACC U CAACCCGC	1372	GCGGGUUG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGUCCCAA	8772
2985	GGGACCUC A ACCCGCAC	1373	GUGCGGGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAGGUCCC	8773
2988	ACCUCAAC C CGCACAAAG	1374	CUUGUGCG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUGAGGU	8774
2989	CCUCAACC C GCACAAGG	1375	CCUUGUGC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGUUGAGG	8775
2992	CAACCCGC A CAAGGACA	1376	UGUCCUUG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICGGGUUG	8776
2994	ACCCGCAC A AGGACAAC	1377	GUUGUCCU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUGCGGUU	8777
3000	ACAAGGAC A ACUGGCCG	1378	CGGCCAGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUCCUUGU	8778
3003	AGGACAAC U GGCCGGAC	1379	GUCCGGCC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUGUCCU	8779
3007	CAACUGGC C GGACGCCA	1380	UGGCGUCC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCAGUUG	8780
3014	CCGGACGC C AACAAAGGU	1381	ACCUUGUU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICGUCCGG	8781
3015	CGGACGCC A ACAAGGUG	1382	CACCUUGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICGUCCGG	8782
3018	ACGCCAAC A AGGUGGGA	1383	UCCCACCU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUGGCGU	8783
3035	GUGGGAGC A UUCGGGCC	1384	GGCCCGAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICUCCAC	8784
3043	AUUCGGGC C AGGGUUCA	1385	UGAACCCU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCCGAAU	8785
3044	UUCGGGCC A GGGUUCAC	1386	GUGAACCC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCCCGAA	8786
3051	CAGGGUUC A CCCUCCCC	1387	GGGAGGGG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAACCCUG	8787
3053	GGGUUCAC C CUCCCCA	1388	UGGGGAGG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUGAACCC	8788
3054	GGUUCACC C CUCCCCAU	1389	AUGGGGAG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGUGAAC	8789
3055	GUUCACCC C UCCCCAUG	1390	CAUGGGGA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGUGAAC	8790
3056	UUCACCCC U CCCCAUGG	1391	CCAUGGGG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGGUGAA	8791
3058	CACCCUC C CCAUGGGG	1392	CCCCAUGG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAGGGGUG	8792
3059	ACCCUCC C CAUGGGGG	1393	CCCCAUG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGAGGGGU	8793
3060	CCCCUCC C AUGGGGGA	1394	UCCCCAU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGAGGGG	8794
3061	CCUCCCC A UGGGGGAC	1395	GUCCCCCA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGAGGGG	8795
3070	UGGGGGAC U GUUGGGGU	1396	ACCCCAAC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUCCCCCA	8796
3084	GGUGGAGC C CUCACGCU	1397	AGCGUGAG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICUCCACC	8797
3085	GUGGAGCC C UCACGCUC	1398	GAGCGUGA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCUCCAC	8798
3086	UGGAGCCC U CACGCUCA	1399	UGAGCGUG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGCUCCA	8799
3088	GAGCCUC A CGCUCAGG	1400	CCUGAGCG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAGGCUC	8800
3092	CCUCACGC U CAGGGCCU	1401	AGGCCUC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICUGAGG	8801
3094	UCACGCUC A GGGCCUAC	1402	GUAGGCC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAGCGUGA	8802
3099	CUCAGGGC C UACUCACA	1403	UGUGAGUA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCUGAG	8803
3100	UCAGGGCC U ACUCACAA	1404	UUGUGAGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCCUGA	8804
3103	GGGCCUAC U CACAACUG	1405	CAGUUGUG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUAGGCCC	8805
3105	GCCUACUC A CAACUGUG	1406	CACAGUUG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAGUAGGC	8806
3107	CUACUCAC A ACUGUGCC	1407	GGCACAGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUAGUAG	8807
3110	CUCACAAC U GUGCCAGC	1408	GCUGGCAC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUGUGAG	8808
3115	AACUGUGC C AGCAGCUC	1409	GAGCUCU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICACAGUU	8809
3116	ACUGUGCC A GCAGCUC	1410	GGAGCUGC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCACAGU	8810

3119	GUGCCAGC A GCUCCUCC	1411	GGAGGAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGGCAC	8811
3122	CCAGCAGC U CCUCCUCC	1412	GGAGGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGCUGG	8812
3124	AGCAGCUC C UCCUCCUG	1413	CAGGAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCUGCU	8813
3125	GCAGCUC U CCUCCUGC	1414	GCAGGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGCUGC	8814
3127	AGCUCUCC C UCCUGCCU	1415	AGGCAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAGCU	8815
3128	GCUCCUCC U CCUGCCUC	1416	GAGGCAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGAGC	8816
3130	UCCUCCUC C UGCCUCCA	1417	UGGAGGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAGGA	8817
3131	CCUCCUCC U GCCUCCAC	1418	GUGGAGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGAGG	8818
3134	CCUCCUGC C UCCACCAA	1419	UUGGUGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGAGG	8819
3135	CUCUGCC U CCACCAAU	1420	AUUGGUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAGGAG	8820
3137	CCUGCCUC C ACCAAUCG	1421	CGAUUGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGCAGG	8821
3138	CUGCCUCC A CCAAUCGG	1422	CCGAUUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGCAG	8822
3140	GCCUCCAC C AAUCGGCA	1423	UGCCGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGAGGC	8823
3141	CCUCCACC A AUCGGCAG	1424	CUGCCGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGAGG	8824
3148	CAAUCGGC A GUCAGGAA	1425	UUCUGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCGAUUG	8825
3152	CGGCAGUC A GGAAGGCA	1426	UGCCUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACUGCCG	8826
3160	AGGAAGGC A GCCUACUC	1427	GAGUAGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUCCU	8827
3163	AAGGCAGC C UACUCCU	1428	AGGGAGUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGCCU	8828
3164	AGGCAGCC U ACUCCUU	1429	AAGGGAGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCUGCCU	8829
3167	CAGCCUAC U CCCUUAUC	1430	GAUAAGGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAGGCUG	8830
3169	GCCUACUC C CUUAUCUC	1431	GAGAUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUAGGC	8831
3170	CCUACUCC C UUAUCUCC	1432	GGAGAUAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUAGG	8832
3171	CUACUCC U UAUCUCCA	1433	UGGAGUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGAGUAG	8833
3176	CCCUUAUC U CCACCUCU	1434	AGAGGUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUAGGG	8834
3178	CUUAUCUC C ACCUCUAA	1435	UUAGAGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAUAG	8835
3179	UUAUCUCC A CCUCUAG	1436	CUUAGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUAA	8836
3181	AUCUCCAC C UCUAAGGG	1437	CCCUAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGAGAU	8837
3182	UCUCCACC U CUAAGGGA	1438	UCCCUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGAGA	8838
3184	UCCACCUC U AAGGGACA	1439	UGUCCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGUGGA	8839
3192	UAAGGGAC A CUCAUCCU	1440	AGGAUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCCUUA	8840
3194	AGGGACAC U CAUCCUCA	1441	UGAGGAUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGUCCU	8841
3196	GGACACUC A UCCUCAGG	1442	CCUGAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUGUCC	8842
3199	CACTUCAUC C UCAGGCCA	1443	UGGCCUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGAGUG	8843
3200	ACUCAUCC U CAGGCCAU	1444	AUGGCUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUGAGU	8844
3202	UCAUCCUC A GGCAUGC	1445	GCAUGGCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAUGA	8845
3206	CCUCAGGC C AUGCAGUG	1446	CACUGCAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUGAGG	8846
3207	CUCAGGCC A UGCAGUGG	1447	CCACUGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCCUGAG	8847

Input Sequence = AF100308. Cut Site = CH/.

Stem Length = 8. Core Sequence = CUGAUGAG X CGAA (X = GCCGUUAGGC or other stem II)

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

Underlined region can be any X sequence or linker, as described herein.

"I" stands for Inosine

TABLE VII: HUMAN HBV G-CLEAVER AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	G-cleaver	Seq ID
61	ACUUUCCU G CUGGUGGC	1448	GCCACCAG UGAUG GCAUGCACUAUGC GCG AGGAAAGU	8848
87	GGAACAGU G AGCCCGUC	1449	GCAGGGCU UGAUG GCAUGCACUAUGC GCG ACUGUCC	8849
94	UGAGCCCU G CUCAGAAU	1450	AUUCUGAG UGAUG GCAUGCACUAUGC GCG AGGGCUCA	8850
112	CUGUCUCU G CCAUAUCG	1451	CGAUAUGG UGAUG GCAUGCACUAUGC GCG AGAGACAG	8851
132	AUCUUAUC G AAGACUGG	1452	CCAGUCUU UGAUG GCAUGCACUAUGC GCG GAUAAGAU	8852
153	CCUGUACC G AACAUCCA	1453	UCCAUGUU UGAUG GCAUGCACUAUGC GCG GGUACAGG	8853
169	AGAAACUC G CAUCAGGA	1454	UCCUGAUG UGAUG GCAUGCACUAUGC GCG GAUGUUCU	8854
192	GGACCCCU G CUCGUGUU	1455	AACACGAG UGAUG GCAUGCACUAUGC GCG AGGGGUCC	8855
222	UUCUUGUU G AAAAAAU	1456	AUUUUUGU UGAUG GCAUGCACUAUGC GCG AACAAAGAA	8856
315	CAAAAUUC G CAGUCCCA	1457	UGGGACUG UGAUG GCAUGCACUAUGC GCG GAAUUUUG	8857
374	UGGUUAUC G CUGGAUGU	1458	ACAUCCAG UGAUG GCAUGCACUAUGC GCG GAUAACCA	8858
387	AUGUGUCU G CGGCGUUU	1459	AAACGCCG UGAUG GCAUGCACUAUGC GCG AGACACAU	8859
410	CUUCCUCU G CAUCCUGC	1460	GCAGGAUG UGAUG GCAUGCACUAUGC GCG AGAGGAAG	8860
417	UGCAUCCU G CUGCUAUG	1461	CAUAGCAG UGAUG GCAUGCACUAUGC GCG AGGAUGCA	8861
420	AUCCUGCU G CUAUGCCU	1462	AGGCAUAG UGAUG GCAUGCACUAUGC GCG AGCAGGAU	8862
425	GCUGCUAU G CCUCAUCU	1463	AGAUGAGG UGAUG GCAUGCACUAUGC GCG AUAGCAGC	8863
468	GGUAUGUU G CCCGUUUG	1464	CAAACGGG UGAUG GCAUGCACUAUGC GCG AACAUACC	8864
518	CGGACCAU G CAAAACCU	1465	AGGUUUUG UGAUG GCAUGCACUAUGC GCG AUGGUCCG	8865
527	CAAAACCU G CACAACUC	1466	GAGUUGUG UGAUG GCAUGCACUAUGC GCG AGGUUUUG	8866
538	CAACUCCU G CUCAAGGA	1467	UCCUUGAG UGAUG GCAUGCACUAUGC GCG AGGAGUUG	8867
569	CUCAUGUU G CUGUACAA	1468	UUGUACAG UGAUG GCAUGCACUAUGC GCG AACAUAGAG	8868
596	CGGAAACU G CACCUGUA	1469	UACAGGUG UGAUG GCAUGCACUAUGC GCG AGUUUCCG	8869
631	GGGCUUUC G CAAAUAUC	1470	GUUUUUUG UGAUG GCAUGCACUAUGC GCG GAAAGCCC	8870
687	UUACUAGU G CCAUUUGU	1471	ACAAAUGG UGAUG GCAUGCACUAUGC GCG ACUAGUAA	8871
747	AUAUGGAU G AUGUGGUU	1472	AACCACAU UGAUG GCAUGCACUAUGC GCG AUCCAUAU	8872
783	AACAUCUU G AGUCCCUU	1473	AAGGGACU UGAUG GCAUGCACUAUGC GCG AAGAUGUU	8873
795	CCCUUUAU G CCGCUGUU	1474	AACAGCGG UGAUG GCAUGCACUAUGC GCG AUAAGGGG	8874
798	UUUAUGCC G CUGUUAAC	1475	GGUAACAG UGAUG GCAUGCACUAUGC GCG GGCAUAAA	8875
911	GGCAUAU G CCACAGGA	1476	UCCUGUGG UGAUG GCAUGCACUAUGC GCG AAUGUGCC	8876
978	GGCCUAU G AUUGGAAA	1477	UUUCCAUU UGAUG GCAUGCACUAUGC GCG AAUAGGCC	8877
997	AUGUCAAC G AAUGUGG	1478	CCACAAUU UGAUG GCAUGCACUAUGC GCG GUUGACAU	8878
1020	UGGGGUUU G CCGCCCUU	1479	AGGGGCGG UGAUG GCAUGCACUAUGC GCG AAACCCCA	8879
1023	GGUUUGCC G CCCCUUUC	1480	GAAAGGGG UGAUG GCAUGCACUAUGC GCG GGCAAACC	8880
1034	CCUUUCAC G CAAUGUGG	1481	CCACAUUG UGAUG GCAUGCACUAUGC GCG GUGAAAGG	8881
1050	GAUAUUCU G CUUUAUUG	1482	CAUUAAGG UGAUG GCAUGCACUAUGC GCG AGAAUAUC	8882
1058	GCUUUAU G CCUUUAUA	1483	UAUAAAGG UGAUG GCAUGCACUAUGC GCG AUUAAAGC	8883
1068	CUUUAUAU G CAUGCAUA	1484	UAUGCAUG UGAUG GCAUGCACUAUGC GCG AUAUAAAG	8884
1072	AUAUGCAU G CAUACAAG	1485	CUUGUAUG UGAUG GCAUGCACUAUGC GCG AUGCAUAU	8885
1103	ACUUUCUC G CCAACUUA	1486	UAAGUUGG UGAUG GCAUGCACUAUGC GCG GAGAAAGU	8886
1139	CAGUAUGU G AACCUUUA	1487	UAAAGGUU UGAUG GCAUGCACUAUGC GCG ACAUACUG	8887
1155	ACCCCGUU G CUCGGCAA	1488	UUGCCGAG UGAUG GCAUGCACUAUGC GCG AACGGGGU	8888
1177	UGGUCUAU G CCAAGUGU	1489	ACACUUGG UGAUG GCAUGCACUAUGC GCG AUAGACCA	8889
1188	AAGUGUUU G CUGACGCA	1490	UGCGUCAG UGAUG GCAUGCACUAUGC GCG AAACACUU	8890
1191	UGUUUGCU G ACGCAACC	1491	GGUUGCGU UGAUG GCAUGCACUAUGC GCG AGCAAACA	8891
1194	UUGCUGAC G CAACCCCC	1492	GGGGGUUG UGAUG GCAUGCACUAUGC GCG GUCAGCAA	8892
1234	CCAUCAGC G CAUGCGUG	1493	CACGCAUG UGAUG GCAUGCACUAUGC GCG GCUGAUGG	8893
1238	CAGCGCAU G CGUGGAAC	1494	GUUCCACG UGAUG GCAUGCACUAUGC GCG AUGCGCUG	8894

1262	UCUCCUCU G CCGAUCCA	1495	UGGAUCGG UGAUG GCAUGCACUAUGC GCG AGAGGAGA	8895
1265	CCUCUGCC G AUCCAUAAC	1496	GUAUGGAU UGAUG GCAUGCACUAUGC GCG GGCAGAGG	8896
1275	UCCAUACC G CGGAACUC	1497	GAGUUCGG UGAUG GCAUGCACUAUGC GCG GGUAUGGA	8897
1290	UCCUAGCC G CUUGUUUU	1498	AAAACAAG UGAUG GCAUGCACUAUGC GCG GGCUAGGA	8898
1299	CUUGUUUU G CUCGCAGC	1499	GCUGCGAG UGAUG GCAUGCACUAUGC GCG AAAACAAG	8899
1303	UUUUGCUC G CAGCAGGU	1500	ACCUGCUG UGAUG GCAUGCACUAUGC GCG GAGCAAAA	8900
1335	UCGGGACU G ACAAUUCU	1501	AGAAUUGU UGAUG GCAUGCACUAUGC GCG AGUCCCGA	8901
1349	UCUGUCGU G CUCUCCCG	1502	CGGGAGAG UGAUG GCAUGCACUAUGC GCG ACGACAGA	8902
1357	GCUCUCCC G CAAUAUA	1503	UAUAUUGU UGAUG GCAUGCACUAUGC GCG GGGAGAGC	8903
1382	CCAUGGCU G CUAGGCUG	1504	CAGCCUAG UGAUG GCAUGCACUAUGC GCG AGCCAUGG	8904
1392	UAGGCUGU G CUGCCAAC	1505	GUUGGCAG UGAUG GCAUGCACUAUGC GCG ACAGCCUA	8905
1395	GCUGUGCU G CCAACUGG	1506	CCAGUUGG UGAUG GCAUGCACUAUGC GCG AGCACAGC	8906
1411	GAUCCUAC G CGGGACGU	1507	ACGUCCCG UGAUG GCAUGCACUAUGC GCG GUAGGAUC	8907
1442	CCGUCGGC G CUGAAUCC	1508	GGAUUCAG UGAUG GCAUGCACUAUGC GCG GCCGACGG	8908
1445	UCGGGCGU G AAUCCCGC	1509	GCGGGAU UGAUG GCAUGCACUAUGC GCG AGCGCCGA	8909
1452	UGAAUCCC G CGGACGAC	1510	GUCGUCCG UGAUG GCAUGCACUAUGC GCG GGGAUUA	8910
1458	CCGCGGAC G ACCCCUCC	1511	GGAGGGGU UGAUG GCAUGCACUAUGC GCG GUCCGCGG	8911
1474	CCGGGGCC G CUUGGGGC	1512	GCCCCAAG UGAUG GCAUGCACUAUGC GCG GGCCCCGG	8912
1489	GCUCUACC G CCCGUUC	1513	GAAGCGGG UGAUG GCAUGCACUAUGC GCG GGUAGAGC	8913
1493	UACCGCCC G CUUCUCCG	1514	CGGAGAAG UGAUG GCAUGCACUAUGC GCG GGGCGGUA	8914
1501	GCUUCUCC G CCUAUUGU	1515	ACAAUAGG UGAUG GCAUGCACUAUGC GCG GGAGAAGC	8915
1513	AUUGUACC G ACCGUCCA	1516	UGGACGGU UGAUG GCAUGCACUAUGC GCG GGUACAAU	8916
1528	CACGGGGC G CACCUCUC	1517	GAGAGGUG UGAUG GCAUGCACUAUGC GCG GCCCCGUG	8917
1542	CUCUUUAC G CGGACUCC	1518	GGAGUCCG UGAUG GCAUGCACUAUGC GCG GUAAAGAG	8918
1559	CCGUCUGU G CCUUCUCA	1519	UGAGAAGG UGAUG GCAUGCACUAUGC GCG ACAGACGG	8919
1571	UCUCAUCU G CCGGACCG	1520	CGGUCCGG UGAUG GCAUGCACUAUGC GCG AGAUGAGA	8920
1583	GACCGUGU G CACUUCGC	1521	GCGAAGUG UGAUG GCAUGCACUAUGC GCG ACACGGUC	8921
1590	UGCACUUC G CUUCACCU	1522	AGGUGAAG UGAUG GCAUGCACUAUGC GCG GAAGUGCA	8922
1601	UCACCUCU G CACGUCGC	1523	GCGACGUG UGAUG GCAUGCACUAUGC GCG AGAGGUGA	8923
1608	UGCACGUC G CAUGGAGA	1524	UCUCCAUG UGAUG GCAUGCACUAUGC GCG GACGUGCA	8924
1624	ACCACCGU G AACGCCCCA	1525	UGGGCGUU UGAUG GCAUGCACUAUGC GCG ACGGUGGU	8925
1628	CCGUGAAC G CCCACAGG	1526	CCUGUGGG UGAUG GCAUGCACUAUGC GCG GUUCACGG	8926
1642	AGGAACCU G CCCAAGGU	1527	ACCUUGGG UGAUG GCAUGCACUAUGC GCG AGGUUCCU	8927
1654	AAGGUCUU G CAUAAGAG	1528	CUCUUAUG UGAUG GCAUGCACUAUGC GCG AAGACCUU	8928
1690	AUGUCAAC G ACCGACCU	1529	AGGUCGGU UGAUG GCAUGCACUAUGC GCG GUUGACAU	8929
1694	CAACGACC G ACCUUGAG	1530	CUCAAGGU UGAUG GCAUGCACUAUGC GCG GGUCGUUG	8930
1700	CCGACCUU G AGGCAUAC	1531	GUAUGCCU UGAUG GCAUGCACUAUGC GCG AAGGUCGG	8931
1730	UGUUAAU G AGUGGGAG	1532	CUCCCAU UGAUG GCAUGCACUAUGC GCG AUUAAACA	8932
1818	AGCACCAU G CAACUUUU	1533	AAAAGUUG UGAUG GCAUGCACUAUGC GCG AUGGUGCU	8933
1835	UCACCUCU G CCUAAUCA	1534	UGAUUAGG UGAUG GCAUGCACUAUGC GCG AGAGGUGA	8934
1883	CAAGCUGU G CCUUGGGU	1535	ACCCAAGG UGAUG GCAUGCACUAUGC GCG ACAGCUUG	8935
1912	UGGACAUU G ACCCGUAA	1536	AUACGGGU UGAUG GCAUGCACUAUGC GCG AAUGUCCA	8936
1959	UCUUUUU G CCUUCUGA	1537	UCAGAAGG UGAUG GCAUGCACUAUGC GCG AAAAAGA	8937
1966	UGCCUUCU G ACUUCUUU	1538	AAAGAAGU UGAUG GCAUGCACUAUGC GCG AGAAGGCA	8938
1985	UUCUAUUC G AGAUCUCC	1539	GGAGAUCU UGAUG GCAUGCACUAUGC GCG GAUAAGAA	8939
1996	AUCUCCUC G ACACCGCC	1540	GGCGGUGU UGAUG GCAUGCACUAUGC GCG GAGGAGAU	8940
2002	UCGACACC G CCUCUGCU	1541	AGCAGAGG UGAUG GCAUGCACUAUGC GCG GGUGUCGA	8941
2008	CCGCCUCU G CUCUGUAA	1542	AUACAGAG UGAUG GCAUGCACUAUGC GCG AGAGGCGG	8942
2092	GUUGGGGU G AGUUGAUG	1543	CAUCAACU UGAUG GCAUGCACUAUGC GCG ACCCCAAC	8943
2097	GGUGAGUU G AUGAAUCU	1544	AGAUUCAU UGAUG GCAUGCACUAUGC GCG AACUCACC	8944
2100	GAGUUGAU G AAUCUAGC	1545	GCUAGAUU UGAUG GCAUGCACUAUGC GCG AUCAACUC	8945

2237	UUUUGGGC G AGAAACUG	1546	CAGUUUCU UGAUG	GCAUGCACUAUGC	GCG GCCCAAAA	8946
2251	CUGUUCUU G AAUAUUUG	1547	CAAAUAUU UGAUG	GCAUGCACUAUGC	GCG AAGAACAG	8947
2282	GUGGAUUC G CACUCCUC	1548	GAGGAGUG UGAUG	GCAUGCACUAUGC	GCG GAAUCCAC	8948
2293	CUCCUCCU G CAUAUAGA	1549	UCUAUAUG UGAUG	GCAUGCACUAUGC	GCG AGGAGGAG	8949
2311	CACCAAAU G CCCCUAUC	1550	GAUAGGGG UGAUG	GCAUGCACUAUGC	GCG AUUUGGUG	8950
2354	UGUUAGAC G AAGAGGCA	1551	UGCCUCUU UGAUG	GCAUGCACUAUGC	GCG GUCUAACA	8951
2388	ACUCCUC G CCUCGCAG	1552	CUGCGAGG UGAUG	GCAUGCACUAUGC	GCG GAGGGAGU	8952
2393	CUCGCCUC G CAGACGAA	1553	UUCGUCUG UGAUG	GCAUGCACUAUGC	GCG GAGGCGAG	8953
2399	UCGCAGAC G AAGGUCUC	1554	GAGACCUU UGAUG	GCAUGCACUAUGC	GCG GUCUGCGA	8954
2412	UCUCAUUC G CCGCGUCG	1555	CGACGCGG UGAUG	GCAUGCACUAUGC	GCG GAUUGAGA	8955
2415	CAAUCGCC G CGUCGCAG	1556	CUGCGACG UGAUG	GCAUGCACUAUGC	GCG GGCGAUUG	8956
2420	GCCGCGUC G CAGAAGAU	1557	AUCUUCUG UGAUG	GCAUGCACUAUGC	GCG GACGCGGC	8957
2514	GGUACCUU G CUUUAUUC	1558	GAUUAAG UGAUG	GCAUGCACUAUGC	GCG AAGGUACC	8958
2549	CUUUUCCU G ACAUUCAU	1559	AUGAAUGU UGAUG	GCAUGCACUAUGC	GCG AGGAAAAG	8959
2560	AUUCAUUU G CAGGAGGA	1560	UCCUCCUG UGAUG	GCAUGCACUAUGC	GCG AAAUGAAU	8960
2576	ACAUUGUU G AUAGAUGU	1561	ACAUCUUA UGAUG	GCAUGCACUAUGC	GCG AACAAUGU	8961
2615	CAGUAAAU G AAAACAGG	1562	CCUGUUUU UGAUG	GCAUGCACUAUGC	GCG AUUUACUG	8962
2641	UUAACUUA G CCUGCUAG	1563	CUAGCAGG UGAUG	GCAUGCACUAUGC	GCG AUAGUUA	8963
2645	CUAUGCCU G CUAGGUUU	1564	AAACCUAG UGAUG	GCAUGCACUAUGC	GCG AGGCAUAG	8964
2677	AAAUAUUU G CCCUAGA	1565	UCUAAGGG UGAUG	GCAUGCACUAUGC	GCG AAAUAUUU	8965
2740	UUCGAGAC G CGACAUAU	1566	UAAUGUCG UGAUG	GCAUGCACUAUGC	GCG GUCUGGAA	8966
2742	CCAGACGC G ACAUUAUU	1567	AAUAAUGU UGAUG	GCAUGCACUAUGC	GCG GCUCUGG	8967
2804	CACGUAGC G CCUCAUUU	1568	AAUAGAGG UGAUG	GCAUGCACUAUGC	GCG GCUACGUG	8968
2814	CUCAUUUU G CGGUCAC	1569	GUGACCCG UGAUG	GCAUGCACUAUGC	GCG AAAAUGAG	8969
2875	CAAACCUC G AAAAGGCA	1570	UGCCUUUU UGAUG	GCAUGCACUAUGC	GCG GAGGUUUG	8970
2928	UCUCCCC G AUCAUCAG	1571	CUGAUGAU UGAUG	GCAUGCACUAUGC	GCG GGGGAAGA	8971
2946	UGGACCCU G CAUUCAAA	1572	UUUGAUG UGAUG	GCAUGCACUAUGC	GCG AGGGUCCA	8972
2990	CUCAACCC G CACAAGGA	1573	UCCUUGUG UGAUG	GCAUGCACUAUGC	GCG GGGUUGAG	8973
3012	GGCCGGAC G CCAACAAG	1574	CUUGUUGG UGAUG	GCAUGCACUAUGC	GCG GUCCGGCC	8974
3090	GCCCUCAC G CUCAGGGC	1575	GCCCUGAG UGAUG	GCAUGCACUAUGC	GCG GUGAGGGC	8975
3113	ACAACUGU G CCAGCAGC	1576	GCUCUGG UGAUG	GCAUGCACUAUGC	GCG ACAGUUGU	8976
3132	CUCCUCCU G CCUCCACC	1577	GGUGGAGG UGAUG	GCAUGCACUAUGC	GCG AGGAGGAG	8977
51	AGGGCCCU G UACUUUCC	1578	GGAAAGUA UGAUG	GCAUGCACUAUGC	GCG AGGGCCCU	8978
106	AGAAUACU G UCUCUGCC	1579	GGCAGAGA UGAUG	GCAUGCACUAUGC	GCG AGUAUUCU	8979
148	GGGACCCU G UACCGAAC	1580	GUUCGGUA UGAUG	GCAUGCACUAUGC	GCG AGGGUCCC	8980
198	CUGCUCGU G UUACAGGC	1581	GCCUGUAA UGAUG	GCAUGCACUAUGC	GCG ACGAGCAG	8981
219	UUUUUCUU G UUGACAAA	1582	UUUGUCAA UGAUG	GCAUGCACUAUGC	GCG AAGAAAAA	8982
297	ACACCCGU G UGUUUGG	1583	CCAAGACA UGAUG	GCAUGCACUAUGC	GCG ACGGGUGU	8983
299	ACCCGUGU G UCUGGGCC	1584	GGCCAAGA UGAUG	GCAUGCACUAUGC	GCG ACACGGGU	8984
347	ACCAACCU G UUGUCCUC	1585	GAGGACAA UGAUG	GCAUGCACUAUGC	GCG AGGUUGGU	8985
350	AACCUGUU G UCCUCCAA	1586	UUGGAGGA UGAUG	GCAUGCACUAUGC	GCG AACAGGUU	8986
362	UCCAAUUU G UCCUGGUU	1587	AACCAGGA UGAUG	GCAUGCACUAUGC	GCG AAUUGGA	8987
381	CGCUGGAU G UGUCUGCG	1588	CGCAGACA UGAUG	GCAUGCACUAUGC	GCG AUCCAGCG	8988
383	CUGGAUGU G UCUGCGGC	1589	GCCGCAGA UGAUG	GCAUGCACUAUGC	GCG ACAUCCAG	8989
438	AUCUUCUU G UUGGUUCU	1590	AGAACCAA UGAUG	GCAUGCACUAUGC	GCG AAGAAGAU	8990
465	CAAGGUUAU G UUGCCCGU	1591	ACGGGCAA UGAUG	GCAUGCACUAUGC	GCG AUACCUUG	8991
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555	ACCUCUAU G UUUCCUC	1593	GAGGGAAA UGAUG	GCAUGCACUAUGC	GCG AUAGAGGU	8993
566	UCCUCUAU G UUGUGUA	1594	UACAGCAA UGAUG	GCAUGCACUAUGC	GCG AUGAGGGA	8994
572	AUGUUGCU G UACAAAC	1595	GUUUUGUA UGAUG	GCAUGCACUAUGC	GCG AGCAACAU	8995
602	CUGCACCU G UAUUCCCA	1596	UGGGAAUA UGAUG	GCAUGCACUAUGC	GCG AGGUGCAG	8996

694	UGCCAUUU G UUCAGUGG	1597	CCACUGAA UGAUG GCAUGCACUAUGC GCG AAAUGGCA	8997
724	CCCCCACU G UCUGGCUU	1598	AAGCCAGA UGAUG GCAUGCACUAUGC GCG AGUGGGGG	8998
750	UGGAUGAU G UGGUUUUG	1599	CAAAACCA UGAUG GCAUGCACUAUGC GCG AUCAUCCA	8999
771	CCAAGUCU G UACAACAU	1600	AUGUUGUA UGAUG GCAUGCACUAUGC GCG AGACUUGG	9000
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818	UUUCUUUU G UCUUUGGG	1602	CCCAAAGA UGAUG GCAUGCACUAUGC GCG AAAAGAAA	9002
888	UGGGAUUAU G UAAUUGGG	1603	CCCAAUUA UGAUG GCAUGCACUAUGC GCG AUUACCCA	9003
927	AACAUAAU G UACAAAAA	1604	UUUUUGUA UGAUG GCAUGCACUAUGC GCG AAUAUGUU	9004
944	AUCAAAAU G UGUUUUAG	1605	CUAAAAACA UGAUG GCAUGCACUAUGC GCG AUUUUGAU	9005
946	CAAAAUUGU G UUUUAGGA	1606	UCCUAAAA UGAUG GCAUGCACUAUGC GCG ACAUUUUG	9006
963	AACUCCCU G UAAACAGG	1607	CCUGUUUA UGAUG GCAUGCACUAUGC GCG AGGAAGUU	9007
991	GAAAGUAU G UCAACGAA	1608	UUCGUUGA UGAUG GCAUGCACUAUGC GCG AUACUUUC	9008
1002	AACGAAAU G UGGGUCUU	1609	AAGACCCA UGAUG GCAUGCACUAUGC GCG AAUUCGUU	9009
1039	CACGCAAU G UGGAUAAU	1610	AAUAUCCA UGAUG GCAUGCACUAUGC GCG AUUGCGUG	9010
1137	AACAGUAU G UGAACCUU	1611	AAGGUUCA UGAUG GCAUGCACUAUGC GCG AUACUGUU	9011
1184	UGCCAAGU G UUGUCUGA	1612	UCAGCAAA UGAUG GCAUGCACUAUGC GCG ACUUGGCA	9012
1251	GAACCUUU G UGUCUCCU	1613	AGGAGACA UGAUG GCAUGCACUAUGC GCG AAAGGUUC	9013
1253	ACCUUUUGU G UCUCUCU	1614	AGAGGAGA UGAUG GCAUGCACUAUGC GCG ACAAGGUU	9014
1294	AGCCGCUU G UUUUGCUC	1615	GAGCAAAA UGAUG GCAUGCACUAUGC GCG AAGCGGCU	9015
1344	ACAAUUCU G UCGUGCUC	1616	GAGCACGA UGAUG GCAUGCACUAUGC GCG AGAAUUGU	9016
1390	GCUAGGCU G UGUGCCA	1617	UGGCAGCA UGAUG GCAUGCACUAUGC GCG AGCCUAGC	9017
1425	CGUCCUUU G UUUACGUC	1618	GACGUAAA UGAUG GCAUGCACUAUGC GCG AAAGGACG	9018
1508	CGCCUAUU G UACCGACC	1619	GGUCGGUA UGAUG GCAUGCACUAUGC GCG AAUAGGCG	9019
1557	CCCCGUCU G UGCCUUCU	1620	AGAAGGCA UGAUG GCAUGCACUAUGC GCG AGACGGGG	9020
1581	CGGACCGU G UGCACUUC	1621	GAAGUGCA UGAUG GCAUGCACUAUGC GCG ACGUCCG	9021
1684	UCAGCAAU G UCAACGAC	1622	GUCGUUGA UGAUG GCAUGCACUAUGC GCG AUUGCUGA	9022
1719	CAAAGACU G UUGUUUA	1623	UAAACACA UGAUG GCAUGCACUAUGC GCG AGUCUUUG	9023
1721	AAGACUGU G UGUUAAU	1624	AUUAAACA UGAUG GCAUGCACUAUGC GCG ACAGUCUU	9024
1723	GACUGUGU G UUUAAUGA	1625	UCAUAAA UGAUG GCAUGCACUAUGC GCG ACACAGUC	9025
1772	AGGUCUUU G UACUAGGA	1626	UCCUAGUA UGAUG GCAUGCACUAUGC GCG AAAGACCU	9026
1785	AGGAGGCU G UAGGCAUA	1627	UAUGCCUA UGAUG GCAUGCACUAUGC GCG AGCCUCCU	9027
1801	AAAUUGGU G UGUUACAC	1628	GGUGAACA UGAUG GCAUGCACUAUGC GCG ACCAAUUU	9028
1803	AUUGGUGU G UUCACCAG	1629	CUGGUGAA UGAUG GCAUGCACUAUGC GCG ACACCAAU	9029
1850	CAUCUCAU G UUCAUGUC	1630	GACAUGAA UGAUG GCAUGCACUAUGC GCG AUGAGAUG	9030
1856	AUGUUCAU G UCCUACUG	1631	CAGUAGGA UGAUG GCAUGCACUAUGC GCG AUGAACAU	9031
1864	GUCCUACU G UUCAAGCC	1632	GGCUUGAA UGAUG GCAUGCACUAUGC GCG AGUAGGAC	9032
1881	UCCAAGCU G UGCCUUGG	1633	CCAAGGCA UGAUG GCAUGCACUAUGC GCG AGCUUGGA	9033
1939	GAGCUUCU G UGGAGUUA	1634	UAACUCCA UGAUG GCAUGCACUAUGC GCG AGAAGCUC	9034
2013	UCUGCUCU G UAUCGGGG	1635	CCCCGAUA UGAUG GCAUGCACUAUGC GCG AGAGCAGA	9035
2045	GGAACAUU G UUCACCUC	1636	GAGGUGAA UGAUG GCAUGCACUAUGC GCG AAUGUCC	9036
2082	GCUAUUCU G UGUUGGGG	1637	CCCCAACA UGAUG GCAUGCACUAUGC GCG AGAAUAGC	9037
2084	UAUUCUGU G UUGGGGUG	1638	CACCCCAA UGAUG GCAUGCACUAUGC GCG ACAGAAUA	9038
2167	UCAGCUAU G UCAACGUU	1639	AACGUUGA UGAUG GCAUGCACUAUGC GCG AUAGCUGA	9039
2205	CAACUAUU G UGGUUUCA	1640	UGAAACCA UGAUG GCAUGCACUAUGC GCG AAUAGUUG	9040
2222	CAUUUCCU G UCUUACUU	1641	AAGUAAGA UGAUG GCAUGCACUAUGC GCG AGGAAAUG	9041
2245	GAGAAACU G UUCUUGAA	1642	UUCAAGAA UGAUG GCAUGCACUAUGC GCG AGUUUCUC	9042
2262	UAUUUGGU G UCUUUGG	1643	CCAAAAGA UGAUG GCAUGCACUAUGC GCG ACCAAAUA	9043
2274	UUUGGAGU G UGGAUUCG	1644	CGAAUCCA UGAUG GCAUGCACUAUGC GCG ACUCCAAA	9044
2344	AAACUACU G UUGUUAGA	1645	UCUAACAA UGAUG GCAUGCACUAUGC GCG AGUAGUUU	9045
2347	CUACUGUU G UUAGACGA	1646	UCGUCUAA UGAUG GCAUGCACUAUGC GCG AACAGUAG	9046
2450	AUCUCAAU G UUGUAUU	1647	AAUACUAA UGAUG GCAUGCACUAUGC GCG AUUGAGAU	9047

2573	AGGACAUU G UUGAUAGA	1648	UCUAUCAA UGAUG GCAUGCACUAUGC GCG AAUGUCCU	9048
2583	UGAUAGAU G UAAGCAAU	1649	AUUGCUUA UGAUG GCAUGCACUAUGC GCG AUCUAUCA	9049
2594	AGCAAUUU G UGGGGCCC	1650	GGGCCCCA UGAUG GCAUGCACUAUGC GCG AAAUUGCU	9050
2663	AUCCCAAU G UUACUAAA	1651	UUUAGUAA UGAUG GCAUGCACUAUGC GCG AUUGGGAU	9051
2717	CAGAGUAU G UAGUUAAU	1652	AUUAACUA UGAUG GCAUGCACUAUGC GCG AUACUCUG	9052
2901	AUCUUUCU G UCCCCAAU	1653	AUUGGGGA UGAUG GCAUGCACUAUGC GCG AGAAAGAU	9053
3071	GGGGGACU G UUGGGGUG	1654	CACCCCAA UGAUG GCAUGCACUAUGC GCG AGUCCCCC	9054
3111	UCACAACU G UGCCAGCA	1655	UGCUGGCA UGAUG GCAUGCACUAUGC GCG AGUUGUGA	9055

Input Sequence = AF100308. Cut Site = YG/M or UG/U.

Stem Length = 8. Core Sequence = UGAUG GCAUGCACUAUGC GCG

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

TABLE VIII: HUMAN HBV ZINZYME AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	Zinzyne	Seq ID
61	ACUUUCCU G CUGGUGGC	1448	GCCACCAG GCcgaagGCGaGuCaaGGuCu AGGAAAGU	9056
94	UGAGCCCU G CUCAGAAU	1450	AUUCUGAG GCcgaagGCGaGuCaaGGuCu AGGGCUCA	9057
112	CUGUCUCU G CCAUAUCG	1451	CGAUAUGG GCcgaagGCGaGuCaaGGuCu AGAGACAG	9058
169	AGAACAUC G CAUCAGGA	1454	UCCUGAUG GCcgaagGCGaGuCaaGGuCu GAUGUUCU	9059
192	GGACCCCU G CUCGUGUU	1455	AACACGAG GCcgaagGCGaGuCaaGGuCu AGGGGUCC	9060
315	CAAAAUUC G CAGUCCCA	1457	UGGGACUG GCcgaagGCGaGuCaaGGuCu GAAUUUUG	9061
374	UGGUUAUC G CUGGAUGU	1458	ACAUCCAG GCcgaagGCGaGuCaaGGuCu GAUAACCA	9062
387	AUGUGUCU G CGGCGUUU	1459	AAACGCCG GCcgaagGCGaGuCaaGGuCu AGACACAU	9063
410	CUUCCUCU G CAUCCUGC	1460	GCAGGAUG GCcgaagGCGaGuCaaGGuCu AGAGGAAG	9064
417	UGCAUCCU G CUGCUAUG	1461	CAUAGCAG GCcgaagGCGaGuCaaGGuCu AGGAUGCA	9065
420	AUCCUGCU G CUAUGCCU	1462	AGGCAUAG GCcgaagGCGaGuCaaGGuCu AGCAGGAU	9066
425	GCUGCUAU G CCUCAUCU	1463	AGAUGAGG GCcgaagGCGaGuCaaGGuCu AUAGCAGC	9067
468	GGUAUGUU G CCCGUUUG	1464	CAAACGGG GCcgaagGCGaGuCaaGGuCu AACAUACC	9068
518	CGGACCAU G CAAAACCU	1465	AGGUUUUG GCcgaagGCGaGuCaaGGuCu AUGGUCCG	9069
527	CAAAACCU G CACAACUC	1466	GAGUUGUG GCcgaagGCGaGuCaaGGuCu AGGUUUUG	9070
538	CAACUCCU G CUCAAGGA	1467	UCCUUGAG GCcgaagGCGaGuCaaGGuCu AGGAGUUG	9071
569	CUCAUGUU G CUGUACAA	1468	UUGUACAG GCcgaagGCGaGuCaaGGuCu AACAUAGG	9072
596	CGGAAACU G CACCUGUA	1469	UACAGGUG GCcgaagGCGaGuCaaGGuCu AGUUUCCG	9073
631	GGGCUUUC G CAAAUAUC	1470	GUUUUUUG GCcgaagGCGaGuCaaGGuCu GAAAGCCC	9074
687	UUACUAGU G CCAUUGUU	1471	ACAAUUGG GCcgaagGCGaGuCaaGGuCu ACUAGUAA	9075
795	CCCUUUAU G CCGCUGUU	1474	AACAGCGG GCcgaagGCGaGuCaaGGuCu AUAAAGGG	9076
798	UUUAUGCC G CUGUUACC	1475	GGUAAACG GCcgaagGCGaGuCaaGGuCu GGCAUAAA	9077
911	GGCACAUC G CCACAGGA	1476	UCCUGUGG GCcgaagGCGaGuCaaGGuCu AAUGUGCC	9078
1020	UGGGGUUU G CCGCCCUU	1479	AGGGGCGG GCcgaagGCGaGuCaaGGuCu AAACCCCA	9079
1023	GGUUUGCC G CCCUJUUC	1480	GAAAGGGG GCcgaagGCGaGuCaaGGuCu GGCAAACC	9080
1034	CCUUUCAC G CAAUGUGG	1481	CCACAUUG GCcgaagGCGaGuCaaGGuCu GUGAAAGG	9081
1050	GAUAUUCU G CUUUAUUG	1482	CAUUAAGG GCcgaagGCGaGuCaaGGuCu AGAAUAUC	9082
1058	GUUUUAU G CCUUUAUA	1483	UAUAAAGG GCcgaagGCGaGuCaaGGuCu AUUAAAGC	9083
1068	CUUUAUUA G CAUGCAUA	1484	UAUGCAUG GCcgaagGCGaGuCaaGGuCu AUUAUAAAG	9084
1072	AUAUGCAU G CAUACAAG	1485	CUUGUAUG GCcgaagGCGaGuCaaGGuCu AUGCAUAU	9085
1103	ACUUUCUC G CCAACUUA	1486	UAAGUUGG GCcgaagGCGaGuCaaGGuCu GAGAAAGU	9086
1155	ACCCCGUU G CUCGGCAA	1488	UUGCCGAG GCcgaagGCGaGuCaaGGuCu AACGGGGU	9087
1177	UGGUCUAU G CCAAGUGU	1489	ACACUUGG GCcgaagGCGaGuCaaGGuCu AUAGACCA	9088
1188	AAGUGUUU G CUGACGCA	1490	UGCGUCAG GCcgaagGCGaGuCaaGGuCu AAACACUU	9089
1194	UUGCUGAC G CAACCCCC	1492	GGGGGUUG GCcgaagGCGaGuCaaGGuCu GUCAGCAA	9090
1234	CCAUCAGC G CAUGCGUG	1493	CACGCAUG GCcgaagGCGaGuCaaGGuCu GCUGAUGG	9091
1238	CAGCGCAU G CGUGGAAC	1494	GUUCCACG GCcgaagGCGaGuCaaGGuCu AUGCGCUG	9092
1262	UCUCCUCU G CCGAUCCA	1495	UGGAUCCG GCcgaagGCGaGuCaaGGuCu AGAGGAGA	9093
1275	UCCAUAAC G CGGAACUC	1497	GAGUUCUG GCcgaagGCGaGuCaaGGuCu GGUAUGGA	9094
1290	UCCUAGCC G CUUGUUUU	1498	AAAACAAG GCcgaagGCGaGuCaaGGuCu GGCUAAGG	9095
1299	CUUGUUUU G CUCGCAGC	1499	GCUGCGAG GCcgaagGCGaGuCaaGGuCu AAAACAAG	9096
1303	UUUUGCUC G CAGCAGGU	1500	ACCUGCUG GCcgaagGCGaGuCaaGGuCu GAGCAAAA	9097
1349	UCUGUCGU G CUCUCCCG	1502	CGGGAGAG GCcgaagGCGaGuCaaGGuCu ACGACAGA	9098
1357	GCUCUCCC G CAAUAUAU	1503	UAUAUUUG GCcgaagGCGaGuCaaGGuCu GGGAGAGC	9099
1382	CCAUGGCU G CUAGGCUG	1504	CAGCCUAG GCcgaagGCGaGuCaaGGuCu AGCCAUGG	9100
1392	UAGGCUGU G CUGCCAAC	1505	GUUGGCAG GCcgaagGCGaGuCaaGGuCu ACAGCCUA	9101
1395	GCUGUCGU G CCAACUGG	1506	CCAGUUGG GCcgaagGCGaGuCaaGGuCu AGCACAGC	9102

1411	GAUCCUAC G CGGGACGU	1507	ACGUCCCG GCcgaagGCGaGuCaaGGuCu	GUAGGAUC	9103
1442	CCGUCGGC G CUGAAUCC	1508	GGAUUCAG GCcgaagGCGaGuCaaGGuCu	GCCGACGG	9104
1452	UGAAUCCC G CGGACGAC	1510	GUCGUCCG GCcgaagGCGaGuCaaGGuCu	GGGAUUCA	9105
1474	CCGGGGCC G CUUGGGGC	1512	GCCCCAAG GCcgaagGCGaGuCaaGGuCu	GGCCCCGG	9106
1489	GCUCUACC G CCCGCUUC	1513	GAAGCGGG GCcgaagGCGaGuCaaGGuCu	GGUAGAGC	9107
1493	UACCGCCC G CUUCUCCG	1514	CGGAGAAG GCcgaagGCGaGuCaaGGuCu	GGGCGGUA	9108
1501	GCUUCUCC G CUAUUGU	1515	ACAAUAGG GCcgaagGCGaGuCaaGGuCu	GGAGAAGC	9109
1528	CACGGGGC G CACCUCUC	1517	GAGAGGUG GCcgaagGCGaGuCaaGGuCu	GCCCCGUG	9110
1542	CUCUUUAC G CGGACUCC	1518	GGAGUCCG GCcgaagGCGaGuCaaGGuCu	GUAAAGAG	9111
1559	CCGUCUGU G CCUUCUCA	1519	UGAGAAGG GCcgaagGCGaGuCaaGGuCu	ACAGACGG	9112
1571	UCUCAUCU G CCGGACCG	1520	CGGUCCGG GCcgaagGCGaGuCaaGGuCu	AGAUGAGA	9113
1583	GACCGUGU G CACUUCGC	1521	GCGAAGUG GCcgaagGCGaGuCaaGGuCu	ACACGGUC	9114
1590	UGCACUUC G CUUACCU	1522	AGGUGAAG GCcgaagGCGaGuCaaGGuCu	GAAGUGCA	9115
1601	UACCCUCU G CACGUCGC	1523	GCGACGUG GCcgaagGCGaGuCaaGGuCu	AGAGGUGA	9116
1608	UGCACGUC G CAUGGAGA	1524	UCUCCAUG GCcgaagGCGaGuCaaGGuCu	GACGUGCA	9117
1628	CCGUGAAC G CCCACAGG	1526	CCUGUGGG GCcgaagGCGaGuCaaGGuCu	GUUCACGG	9118
1642	AGGAACCU G CCCAAGGU	1527	ACCUUGGG GCcgaagGCGaGuCaaGGuCu	AGGUUCCU	9119
1654	AAGGUCUU G CAUAAGAG	1528	CUCUUAUG GCcgaagGCGaGuCaaGGuCu	AAGACCUU	9120
1818	AGCACCAU G CAACUUUU	1533	AAAAGUUG GCcgaagGCGaGuCaaGGuCu	AUGGUGCU	9121
1835	UACCCUCU G CCUAUAUA	1534	UGAUUAGG GCcgaagGCGaGuCaaGGuCu	AGAGGUGA	9122
1883	CAAGCUGU G CCUUGGGU	1535	ACCCAAGG GCcgaagGCGaGuCaaGGuCu	ACAGCUUG	9123
1959	UCUUUUUU G CCUUCUGA	1537	UCAGAAGG GCcgaagGCGaGuCaaGGuCu	AAAAAGA	9124
2002	UCGACACC G CCUCUGCU	1541	AGCAGAGG GCcgaagGCGaGuCaaGGuCu	GGUGUCGA	9125
2008	CCGCCUCU G CUCUGUAU	1542	AUACAGAG GCcgaagGCGaGuCaaGGuCu	AGAGCGGG	9126
2282	GUGGAUUC G CACUCCUC	1548	GAGGAGUG GCcgaagGCGaGuCaaGGuCu	GAUCCAC	9127
2293	CUCCUCCU G CAUAUAGA	1549	UCUAUAUG GCcgaagGCGaGuCaaGGuCu	AGGAGGAG	9128
2311	CACCAAU G CCCUAUC	1550	GAUAGGGG GCcgaagGCGaGuCaaGGuCu	AUUUGGUG	9129
2388	ACUCCUC G CCUCGCAG	1552	CUGCGAGG GCcgaagGCGaGuCaaGGuCu	GAGGAGU	9130
2393	CUCGCCUC G CAGACGAA	1553	UUCGUCUG GCcgaagGCGaGuCaaGGuCu	GAGGCGAG	9131
2412	UCUCAAUC G CCGCGUCG	1555	CGACGCGG GCcgaagGCGaGuCaaGGuCu	GAUUGAGA	9132
2415	CAAUCGCC G CGUCGCAG	1556	CUGCGACG GCcgaagGCGaGuCaaGGuCu	GGCGAUUG	9133
2420	GCCGCGUC G CAGAAGAU	1557	AUCUUCUG GCcgaagGCGaGuCaaGGuCu	GACGCGGC	9134
2514	GGUACCUU G CUUUAUUC	1558	GAUUAAGG GCcgaagGCGaGuCaaGGuCu	AAGGUACC	9135
2560	AUUCAUUU G CAGGAGGA	1560	UCCUCCUG GCcgaagGCGaGuCaaGGuCu	AAAUAGAU	9136
2641	UUAACUAU G CCUGCUAG	1563	CUAGCAGG GCcgaagGCGaGuCaaGGuCu	AUAGUUAA	9137
2645	CUAUGCCU G CUAGGUUU	1564	AAACCUAG GCcgaagGCGaGuCaaGGuCu	AGGCAUAG	9138
2677	AAAUUUUU G CCCUAGA	1565	UCUAAGGG GCcgaagGCGaGuCaaGGuCu	AAAUUUUU	9139
2740	UUCACAGAC G CGACAUUA	1566	UAAUGUCG GCcgaagGCGaGuCaaGGuCu	GUCUGGAA	9140
2804	CACGUAGC G CCUCAUUU	1568	AAAUGAGG GCcgaagGCGaGuCaaGGuCu	GUACGUG	9141
2814	CUCAUUUU G CGGGUCAC	1569	GUGACCCG GCcgaagGCGaGuCaaGGuCu	AAAUGAG	9142
2946	UGGACCCU G CAUUCAAA	1572	UUUGAAUG GCcgaagGCGaGuCaaGGuCu	AGGGUCCA	9143
2990	CUCAACCC G CACAAGGA	1573	UCCUUGUG GCcgaagGCGaGuCaaGGuCu	GGGUUGAG	9144
3012	GGCCGGAC G CCAACAAG	1574	CUUGUUGG GCcgaagGCGaGuCaaGGuCu	GUCCGGCC	9145
3090	GCCUCAC G CUCAGGGC	1575	GCCUCAGG GCcgaagGCGaGuCaaGGuCu	GUGAGGGC	9146
3113	ACAACUGU G CCAGCAGC	1576	GCUGCUGG GCcgaagGCGaGuCaaGGuCu	ACAGUUGU	9147
3132	CUCCUCCU G CCUCCACC	1577	GGUGGAGG GCcgaagGCGaGuCaaGGuCu	AGGAGGAG	9148
51	AGGGCCCU G UACUUUCC	1578	GGAAGUA GCcgaagGCGaGuCaaGGuCu	AGGGCCCU	9149
106	AGAAUACU G UCUCUGCC	1579	GGCAGAGA GCcgaagGCGaGuCaaGGuCu	AGUAUUCU	9150
148	GGGACCCU G UACCGAAC	1580	GUUCGGUA GCcgaagGCGaGuCaaGGuCu	AGGGUCCC	9151
198	CUGCUCGU G UUACAGGC	1581	GCCUGUAA GCcgaagGCGaGuCaaGGuCu	ACGAGCAG	9152
219	UUUUUCUU G UUGACAAA	1582	UUUGUCAA GCcgaagGCGaGuCaaGGuCu	AAGAAAAA	9153

297	ACACCCGU G UGUCUUGG	1583	CCAAGACA GCcgaagGCGaGuCaaGGuCu	ACGGGUGU	9154
299	ACCCGUGU G UCUUGGCC	1584	GGCCAAGA GCcgaagGCGaGuCaaGGuCu	ACACGGGU	9155
347	ACCAACCU G UUGUCCUC	1585	GAGGACAA GCcgaagGCGaGuCaaGGuCu	AGGUUGGU	9156
350	AACCGU G UCCUCCAA	1586	UUGGAGGA GCcgaagGCGaGuCaaGGuCu	AACAGGUU	9157
362	UCCAAUUU G UCCUGGUU	1587	AACCAGGA GCcgaagGCGaGuCaaGGuCu	AAAUUGGA	9158
381	CGCUGGAU G UGUCUGCG	1588	CGCAGACA GCcgaagGCGaGuCaaGGuCu	AUCCAGCG	9159
383	CUGGAUGU G UCUGCGGC	1589	GCCGCAGA GCcgaagGCGaGuCaaGGuCu	ACAUCCAG	9160
438	AUCUUCU G UUGGUUCU	1590	AGAACCAA GCcgaagGCGaGuCaaGGuCu	AAGAAGAU	9161
465	CAAGGUU G UUGCCCGU	1591	ACGGGCAA GCcgaagGCGaGuCaaGGuCu	AUACCUUG	9162
476	GCCCGUUU G UCCUCUAA	1592	UUAGAGGA GCcgaagGCGaGuCaaGGuCu	AAACGGGC	9163
555	ACCUCU G UUCCUC	1593	GAGGAAA GCcgaagGCGaGuCaaGGuCu	AUAGAGGU	9164
566	UCCCUCAU G UUGCUGUA	1594	UACAGCAA GCcgaagGCGaGuCaaGGuCu	AUGAGGGA	9165
572	AUGUUGCU G UACAAAAC	1595	GUUUUGUA GCcgaagGCGaGuCaaGGuCu	AGCAACAU	9166
602	CUGCACCU G UAUUCCA	1596	UGGAAUA GCcgaagGCGaGuCaaGGuCu	AGGUGCAG	9167
694	UGCCAUU G UUCAGUGG	1597	CCACUGAA GCcgaagGCGaGuCaaGGuCu	AAUUGGCA	9168
724	CCCCACU G UCUGGCUU	1598	AAGCCAGA GCcgaagGCGaGuCaaGGuCu	AGUGGGGG	9169
750	UGGAUGAU G UGGUUUUG	1599	CAAAACCA GCcgaagGCGaGuCaaGGuCu	AUCAUCCA	9170
771	CCAAGUCU G UACAACAU	1600	AUGUUGUA GCcgaagGCGaGuCaaGGuCu	AGACUUGG	9171
801	AUGCCGCU G UUACCAU	1601	AUUGGUAA GCcgaagGCGaGuCaaGGuCu	AGCGGCAU	9172
818	UUUCUUU G UCUUUGG	1602	CCCAAAGA GCcgaagGCGaGuCaaGGuCu	AAAAGAAA	9173
888	UGGGAUUA G UAAUUGG	1603	CCCAUUA GCcgaagGCGaGuCaaGGuCu	AUAUCCCA	9174
927	AACAUAU G UACAAAA	1604	UUUUUGUA GCcgaagGCGaGuCaaGGuCu	AAUAUGUU	9175
944	AUAAAAU G UGUUUUAG	1605	CUAAAAA GCcgaagGCGaGuCaaGGuCu	AUUUUGAU	9176
946	CAAAUGU G UUUUAGGA	1606	UCCUAAAA GCcgaagGCGaGuCaaGGuCu	ACAUUUUG	9177
963	AACUUCU G UAAACAGG	1607	CCUGUUUA GCcgaagGCGaGuCaaGGuCu	AGGAAGUU	9178
991	GAAAGUAU G UCAACGAA	1608	UUCGUUGA GCcgaagGCGaGuCaaGGuCu	AUACUUUC	9179
1002	AACGAUU G UGGGUCUU	1609	AAGACCCA GCcgaagGCGaGuCaaGGuCu	AAUUCGUU	9180
1039	CACGCAU G UGGAUAU	1610	AAUAUCCA GCcgaagGCGaGuCaaGGuCu	AUUGCGUG	9181
1137	AACAGUAU G UGAACCUU	1611	AAGGUUCA GCcgaagGCGaGuCaaGGuCu	AUACUGUU	9182
1184	UGCCAAGU G UUGCUGA	1612	UCAGCAAA GCcgaagGCGaGuCaaGGuCu	ACUUGGCA	9183
1251	GAACUUU G UGUCUCU	1613	AGGAGACA GCcgaagGCGaGuCaaGGuCu	AAAGGUUC	9184
1253	ACUUUGU G UCUCUCU	1614	AGAGGAGA GCcgaagGCGaGuCaaGGuCu	ACAAAGGU	9185
1294	AGCCGCU G UUUUGCUC	1615	GAGCAAAA GCcgaagGCGaGuCaaGGuCu	AAGCGGCU	9186
1344	ACAAUUCU G UCGUGCUC	1616	GAGCACGA GCcgaagGCGaGuCaaGGuCu	AGAAUUGU	9187
1390	GUAGGCU G UGCUGCCA	1617	UGGCAGCA GCcgaagGCGaGuCaaGGuCu	AGCCUAGC	9188
1425	CGUCCUU G UUUACGUC	1618	GACGUAAA GCcgaagGCGaGuCaaGGuCu	AAAGGACG	9189
1508	CGCCUAU G UACCGACC	1619	GGUCGUUA GCcgaagGCGaGuCaaGGuCu	AAUAGGCG	9190
1557	CCCCGUCU G UGCCUUCU	1620	AGAAGGCA GCcgaagGCGaGuCaaGGuCu	AGACGGGG	9191
1581	CGGACCGU G UGCACUUC	1621	GAAGUGCA GCcgaagGCGaGuCaaGGuCu	ACGGUCCG	9192
1684	UCAGCAU G UCAACGAC	1622	GUCGUUGA GCcgaagGCGaGuCaaGGuCu	AUUGCUGA	9193
1719	CAAAGACU G UGUGUUUA	1623	UAAACACA GCcgaagGCGaGuCaaGGuCu	AGUCUUUG	9194
1721	AAGACUGU G UGUUUAAU	1624	AUUAAACA GCcgaagGCGaGuCaaGGuCu	ACAGUCUU	9195
1723	GACUGUGU G UUUAAUGA	1625	UCAUAAA GCcgaagGCGaGuCaaGGuCu	ACACAGUC	9196
1772	AGGUUUU G UACUAGGA	1626	UCCUAGUA GCcgaagGCGaGuCaaGGuCu	AAAGACCU	9197
1785	AGGAGGCU G UAGGCAUA	1627	UAUGCCUA GCcgaagGCGaGuCaaGGuCu	AGCCUCCU	9198
1801	AAAUUGGU G UGUUCACC	1628	GGUGAACA GCcgaagGCGaGuCaaGGuCu	ACCAAUUU	9199
1803	AUUGUGU G UUCACCAG	1629	CUGUGUAA GCcgaagGCGaGuCaaGGuCu	ACACCAAU	9200
1850	CAUCUCAU G UUCAUGUC	1630	GACAUGAA GCcgaagGCGaGuCaaGGuCu	AUGAGAUG	9201
1856	AUGUUCU G UCCUACUG	1631	CAGUAGGA GCcgaagGCGaGuCaaGGuCu	AUGAACAU	9202
1864	GUCCUACU G UUCAAGCC	1632	GGCUUGAA GCcgaagGCGaGuCaaGGuCu	AGUAGGAC	9203
1881	UCCAAGCU G UGCCUUGG	1633	CCAAGGCA GCcgaagGCGaGuCaaGGuCu	AGCUUGGA	9204

1939	GAGCUUCU G UGGAGUUA	1634	UAACUCCA GCcgaagGCGaGuCaaGGuCu	AGAAGCUC	9205
2013	UCUGCUCU G UAUCGGGG	1635	CCCCGAUA GCcgaagGCGaGuCaaGGuCu	AGAGCAGA	9206
2045	GGAACAUAU G UUCACCUC	1636	GAGGUGAA GCcgaagGCGaGuCaaGGuCu	AAUGUUC	9207
2082	GCUAUUCU G UGUUGGGG	1637	CCCCAACA GCcgaagGCGaGuCaaGGuCu	AGAAUAGC	9208
2084	UAUUCUGU G UUGGGGUG	1638	CACCCCAA GCcgaagGCGaGuCaaGGuCu	ACAGAAUA	9209
2167	UCAGCUAU G UCAACGUU	1639	AACGUUGA GCcgaagGCGaGuCaaGGuCu	AUAGCUGA	9210
2205	CAACUAUU G UGUUUUCA	1640	UGAAACCA GCcgaagGCGaGuCaaGGuCu	AAUAGUUG	9211
2222	CAUUUCCU G UCUUACUU	1641	AAGUAAGA GCcgaagGCGaGuCaaGGuCu	AGGAAUUG	9212
2245	GAGAAACU G UUCUUGAA	1642	UUCAAGAA GCcgaagGCGaGuCaaGGuCu	AGUUUCUC	9213
2262	UAUUUGGU G UCUUUUGG	1643	CCAAAAGA GCcgaagGCGaGuCaaGGuCu	ACCAAUA	9214
2274	UUUGGAGU G UGGAUUCG	1644	CGAAUCCA GCcgaagGCGaGuCaaGGuCu	ACUCCAAA	9215
2344	AAACUACU G UUGUUAGA	1645	UCUAACAA GCcgaagGCGaGuCaaGGuCu	AGUAGUUU	9216
2347	CUACUGUU G UUAGACGA	1646	UCGUCUAA GCcgaagGCGaGuCaaGGuCu	AACAGUAG	9217
2450	AUCUCAAU G UUAGUAUU	1647	AAUACUAA GCcgaagGCGaGuCaaGGuCu	AUUGAGAU	9218
2573	AGGACAUU G UUGAUAGA	1648	UCUAUCAA GCcgaagGCGaGuCaaGGuCu	AAUGUCCU	9219
2583	UGAUAGAU G UAAGCAAU	1649	AUUGCUUA GCcgaagGCGaGuCaaGGuCu	AUCUAUCA	9220
2594	AGCAAUUU G UGGGGCCC	1650	GGGCCCCA GCcgaagGCGaGuCaaGGuCu	AAAUUGCU	9221
2663	AUCCCAAU G UUACUAAA	1651	UUUAGUAA GCcgaagGCGaGuCaaGGuCu	AUUGGGAU	9222
2717	CAGAGUAU G UAGUUAUU	1652	AUUAACUA GCcgaagGCGaGuCaaGGuCu	AUACUCUG	9223
2901	AUCUUUCU G UCCCCAAU	1653	AUUGGGGA GCcgaagGCGaGuCaaGGuCu	AGAAAGAU	9224
3071	GGGGGACU G UUGGGGUG	1654	CACCCCAA GCcgaagGCGaGuCaaGGuCu	AGUCCCCC	9225
3111	UCACAACU G UGCCAGCA	1655	UGCUGGCA GCcgaagGCGaGuCaaGGuCu	AGUUGUGA	9226
40	AUCCCAGA G UCAGGGCC	1656	GGCCUCGA GCcgaagGCGaGuCaaGGuCu	UCUGGGAU	9227
46	GAGUCAGG G CCCUGUAC	1657	GUACAGGG GCcgaagGCGaGuCaaGGuCu	CCUGACUC	9228
65	UCCUGCUG G UGGCUCCA	1658	UGGAGCCA GCcgaagGCGaGuCaaGGuCu	CAGCAGGA	9229
68	UGCUGGUG G CUCCAGUU	1659	AACUGGAG GCcgaagGCGaGuCaaGGuCu	CACCAGCA	9230
74	UGGCUCCA G UUCAGGAA	1660	UUCUGAA GCcgaagGCGaGuCaaGGuCu	UGGAGCCA	9231
85	CAGGAACA G UGAGCCCU	1661	AGGGUCUA GCcgaagGCGaGuCaaGGuCu	UGUUCUCG	9232
89	AACAGUGA G CCCUGCUC	1662	GAGCAGGG GCcgaagGCGaGuCaaGGuCu	UCACUGUU	9233
120	GCCAUUAC G UCAAUCUU	1663	AAGAUUGA GCcgaagGCGaGuCaaGGuCu	GAUAUGGC	9234
196	CCCUGCUC G UGUUACAG	1664	CUGUAACA GCcgaagGCGaGuCaaGGuCu	GAGCAGGG	9235
205	UGUUAACAG G CGGGGUUU	1665	AAACCCCG GCcgaagGCGaGuCaaGGuCu	CUGUAACA	9236
210	CAGGCGGG G UUUUUCUU	1666	AAGAAAAA GCcgaagGCGaGuCaaGGuCu	CCCGCCUG	9237
248	ACCACAGA G UCUAGACU	1667	AGUCUAGA GCcgaagGCGaGuCaaGGuCu	UCUGUGGU	9238
258	CUAGACUC G UGGUGGAC	1668	GUCCACCA GCcgaagGCGaGuCaaGGuCu	GAGUCUAG	9239
261	GACUCGUG G UGGACUUC	1669	GAAGUCCA GCcgaagGCGaGuCaaGGuCu	CACGAGUC	9240
295	GAACACCC G UGUGUCUU	1670	AAGACACA GCcgaagGCGaGuCaaGGuCu	GGGUGUUC	9241
305	GUGUCUUG G CCAAAAUU	1671	AAUUUUGG GCcgaagGCGaGuCaaGGuCu	CAAGACAC	9242
318	AAUUCGCA G UCCCAAU	1672	AUUUGGGA GCcgaagGCGaGuCaaGGuCu	UGCGAAU	9243
332	AAUCUCCA G UCACUCAC	1673	GUGAGUGA GCcgaagGCGaGuCaaGGuCu	UGGAGAUU	9244
368	UGUUCUG G UUAUCGCU	1674	AGCGAUAA GCcgaagGCGaGuCaaGGuCu	CAGGACAA	9245
390	UGUCUGCG G CGUUUAU	1675	AUAAAACG GCcgaagGCGaGuCaaGGuCu	CGCAGACA	9246
392	UCUGCGGC G UUUUAUCA	1676	UGAUAAAA GCcgaagGCGaGuCaaGGuCu	GCCGCAGA	9247
442	UCUUGUUG G UUCUUCUG	1677	CAGAAGAA GCcgaagGCGaGuCaaGGuCu	CAACAAGA	9248
461	CUAUCAAG G UAUGUUGC	1678	GCAACAUA GCcgaagGCGaGuCaaGGuCu	CUUGAUAG	9249
472	UGUUGCCC G UUUGUCCU	1679	AGGACAAA GCcgaagGCGaGuCaaGGuCu	GGGCAACA	9250
506	AACAACCA G CACCGGAC	1680	GUCCGGUG GCcgaagGCGaGuCaaGGuCu	UGGUUGUU	9251
625	CAUCUUGG G CUUUCGCA	1681	UGCGAAAG GCcgaagGCGaGuCaaGGuCu	CCAAGAU	9252
648	CUAUGGGA G UGGGCCUC	1682	GAGGCCCA GCcgaagGCGaGuCaaGGuCu	UCCCAUAG	9253
652	GGGAGUGG G CCUCAGUC	1683	GACUGAGG GCcgaagGCGaGuCaaGGuCu	CCACUCCC	9254
658	GGGCCUCA G UCCGUUUC	1684	GAAACGGA GCcgaagGCGaGuCaaGGuCu	UGAGGCC	9255

662	CUCAGUCC G UUCUCUU	1685	AAGAGAAA GCcgaagGCGaGuCaaGGuCu	GGACUGAG	9256
672	UUCUCUUG G CUCAGUUU	1686	AAACUGAG GCcgaagGCGaGuCaaGGuCu	CAAGAGAA	9257
677	UUGGCUCA G UUUACUAG	1687	CUAGUAAA GCcgaagGCGaGuCaaGGuCu	UGAGCCAA	9258
685	GUUUACUA G UGCCAUUU	1688	AAAUGGCA GCcgaagGCGaGuCaaGGuCu	UAGUAAAC	9259
699	UUUGUUCA G UGGUUCGU	1689	ACGAACCA GCcgaagGCGaGuCaaGGuCu	UGAACAAA	9260
702	GUUCAGUG G UUCGUAGG	1690	CCUACGAA GCcgaagGCGaGuCaaGGuCu	CACUGAAC	9261
706	AGUGGUUC G UAGGGCUU	1691	AAGCCCUA GCcgaagGCGaGuCaaGGuCu	GAACCACU	9262
711	UUCGUAGG G CUUCCCC	1692	GGGGAAAG GCcgaagGCGaGuCaaGGuCu	CCUACGAA	9263
729	ACUGUCUG G CUUUCAGU	1693	ACUGAAAG GCcgaagGCGaGuCaaGGuCu	CAGACAGU	9264
736	GGCUUUCA G UUAUAUGG	1694	CCAUUAUA GCcgaagGCGaGuCaaGGuCu	UGAAAGCC	9265
753	AUGAUGUG G UUUUGGGG	1695	CCCCAAAA GCcgaagGCGaGuCaaGGuCu	CACAUCAU	9266
762	UUUUGGGG G CCAAGUCU	1696	AGACUUGG GCcgaagGCGaGuCaaGGuCu	CCCCAAAA	9267
767	GGGGCCAA G UCUGUACA	1697	UGUACAGA GCcgaagGCGaGuCaaGGuCu	UUGGCCCC	9268
785	CAUCUUGA G UCCCUUUA	1698	UAAAGGGA GCcgaagGCGaGuCaaGGuCu	UCAAGAUG	9269
826	GUCUUUGG G UAUACAUU	1699	AAUGUAUA GCcgaagGCGaGuCaaGGuCu	CCAAAGAC	9270
898	AAUUGGGA G UUGGGGCA	1700	UGCCCCAA GCcgaagGCGaGuCaaGGuCu	UCCCAAUU	9271
904	GAGUUGGG G CACAUUGC	1701	GCAAUGUG GCcgaagGCGaGuCaaGGuCu	CCCAACUC	9272
971	GUAAACAG G CCUAUUGA	1702	UCAUAGG GCcgaagGCGaGuCaaGGuCu	CUGUUUAC	9273
987	AUUGGAAA G UAUGUCAA	1703	UUGACAUA GCcgaagGCGaGuCaaGGuCu	UUUCCAAU	9274
1006	AAUUGUGG G UCUUUUGG	1704	CCAAAAGA GCcgaagGCGaGuCaaGGuCu	CCACAAUU	9275
1016	CUUUGGGG G UUGCCCGC	1705	GCGGCAAA GCcgaagGCGaGuCaaGGuCu	CCCAAAAG	9276
1080	GCAUACAA G CAAAACAG	1706	CUGUUUUG GCcgaagGCGaGuCaaGGuCu	UUGUAUGC	9277
1089	CAAAACAG G CUUUUACU	1707	AGUAAAAG GCcgaagGCGaGuCaaGGuCu	CUGUUUUG	9278
1116	CUUACAAG G CCUUUCUA	1708	UAGAAAGG GCcgaagGCGaGuCaaGGuCu	CUUGUAAG	9279
1126	CUUUCUAA G UAAACAGU	1709	ACUGUUUA GCcgaagGCGaGuCaaGGuCu	UUAGAAAG	9280
1133	AGUAAACA G UAUGUGAA	1710	UUCACAUA GCcgaagGCGaGuCaaGGuCu	UGUUUACU	9281
1152	UUUACCCC G UUGCUCGG	1711	CCGAGCAA GCcgaagGCGaGuCaaGGuCu	GGGGUAAA	9282
1160	GUUGCUCG G CAACGGCC	1712	GGCCGUUG GCcgaagGCGaGuCaaGGuCu	CGAGCAAC	9283
1166	CGGCAACG G CCUGGUCU	1713	AGACCAGG GCcgaagGCGaGuCaaGGuCu	CGUUGCCG	9284
1171	ACGGCCUG G UCUAUGCC	1714	GGCAUAGA GCcgaagGCGaGuCaaGGuCu	CAGGCCGU	9285
1182	UAUGCCAA G UGUUUGCU	1715	AGCAAACA GCcgaagGCGaGuCaaGGuCu	UUGGCAUA	9286
1207	CCCCACUG G UUGGGGCU	1716	AGCCCCAA GCcgaagGCGaGuCaaGGuCu	CAGUGGGG	9287
1213	UGGUUGGG G CUUGGCCA	1717	UGGCCAAG GCcgaagGCGaGuCaaGGuCu	CCCAACCA	9288
1218	GGGGCUUG G CCAUAGGC	1718	GCCUAUGG GCcgaagGCGaGuCaaGGuCu	CAAGCCCC	9289
1225	GGCCAUAG G CCAUCAGC	1719	GCUGAUGG GCcgaagGCGaGuCaaGGuCu	CUAUGGCC	9290
1232	GGCCAUCA G CGCAUGCG	1720	CGCAUGCG GCcgaagGCGaGuCaaGGuCu	UGAUGGCC	9291
1240	GCGCAUGC G UGGAACCU	1721	AGGUUCCA GCcgaagGCGaGuCaaGGuCu	GCAUGCGC	9292
1287	AACUCCUA G CCGCUUGU	1722	ACAAGCGG GCcgaagGCGaGuCaaGGuCu	UAGGAGUU	9293
1306	UGCUCGCA G CAGGUCUG	1723	CAGACCUG GCcgaagGCGaGuCaaGGuCu	UGCGAGCA	9294
1310	CGCAGCAG G UCUGGGGC	1724	GCCCCAGA GCcgaagGCGaGuCaaGGuCu	CUGCUGCG	9295
1317	GGUCUGGG G CAAAACUC	1725	GAGUUUUG GCcgaagGCGaGuCaaGGuCu	CCCAGACC	9296
1347	AUUCUGUC G UGCUCUCC	1726	GGAGAGCA GCcgaagGCGaGuCaaGGuCu	GACAGAAU	9297
1379	UUUCCAUG G CUGCUAGG	1727	CCUAGCAG GCcgaagGCGaGuCaaGGuCu	CAUGGAAA	9298
1387	GCUGCUAG G CUGUGCUG	1728	CAGCACAG GCcgaagGCGaGuCaaGGuCu	CUAGCAGC	9299
1418	CGCGGGAC G UCCUUGU	1729	ACAAAGGA GCcgaagGCGaGuCaaGGuCu	GUCCCGCG	9300
1431	UUGUUUAC G UCCCGUCG	1730	CGACGGGA GCcgaagGCGaGuCaaGGuCu	GUAAACAA	9301
1436	UACGUCCC G UCGGCGCU	1731	AGCGCCGA GCcgaagGCGaGuCaaGGuCu	GGGACGUA	9302
1440	UCCCGUCG G CGCUGAAU	1732	AUUCAGCG GCcgaagGCGaGuCaaGGuCu	CGACGGGA	9303
1471	CUCCCCGG G CCGCUUGG	1733	CCAAGCGG GCcgaagGCGaGuCaaGGuCu	CCCGGGAG	9304
1481	CGCUUGGG G CUCUACCG	1734	CGGUAGAG GCcgaagGCGaGuCaaGGuCu	CCCAAGCG	9305
1517	UACCGACC G UCCACGGG	1735	CCCGUGGA GCcgaagGCGaGuCaaGGuCu	GGUCGGUA	9306

1526	UCCACGGG G CGCACCUC	1736	GAGGUGCG GCcgaagGCGaGuCaaGGuCu	CCCUGGA	9307
1553	GACUCCCC G UCUGUGCC	1737	GGCACAGA GCcgaagGCGaGuCaaGGuCu	GGGAGUC	9308
1579	GCCGGACC G UGUGCACU	1738	AGUGCACA GCcgaagGCGaGuCaaGGuCu	GGUCCGGC	9309
1605	CUCUGCAC G UCGCAUGG	1739	CCAUGCGA GCcgaagGCGaGuCaaGGuCu	GUGCAGAG	9310
1622	AGACCACC G UGAACGCC	1740	GGCGUUCA GCcgaagGCGaGuCaaGGuCu	GGUGGUCU	9311
1649	UGCCCAAG G UCUUGCAU	1741	AUGCAAGA GCcgaagGCGaGuCaaGGuCu	CUUGGGCA	9312
1679	GACUUUCA G CAAUGUCA	1742	UGACAUUG GCcgaagGCGaGuCaaGGuCu	UGAAAGUC	9313
1703	ACCUUGAG G CAUACUUC	1743	GAAGUAUG GCcgaagGCGaGuCaaGGuCu	CUCAAGGU	9314
1732	UUUAAUGA G UGGGAGGA	1744	UCCUCCCA GCcgaagGCGaGuCaaGGuCu	UCAUAAA	9315
1741	UGGGAGGA G UUGGGGGA	1745	UCCCCCAA GCcgaagGCGaGuCaaGGuCu	UCCUCCCA	9316
1754	GGGAGGAG G UUAGGUUA	1746	UAACCUAA GCcgaagGCGaGuCaaGGuCu	CUCCUCCC	9317
1759	GAGGUUAG G UUAAGGU	1747	ACCUUUAA GCcgaagGCGaGuCaaGGuCu	CUAACCU	9318
1766	GGUAAAAG G UCUUGUA	1748	UACAAAGA GCcgaagGCGaGuCaaGGuCu	CUUUAACC	9319
1782	ACUAGGAG G CUGUAGGC	1749	GCCUACAG GCcgaagGCGaGuCaaGGuCu	CUCCUAGU	9320
1789	GGCUGUAG G CAUAAAUU	1750	AAUUUAUG GCcgaagGCGaGuCaaGGuCu	CUACAGCC	9321
1799	AUAAAUUG G UGUGUUCA	1751	UGAACACA GCcgaagGCGaGuCaaGGuCu	CAAUUUAU	9322
1811	GUUCACCA G CACCAUGC	1752	GCAUGGUG GCcgaagGCGaGuCaaGGuCu	UGGUGAAC	9323
1870	CUGUUCAA G CCUCCAAG	1753	CUUGGAGG GCcgaagGCGaGuCaaGGuCu	UUGAACAG	9324
1878	GCCUCCAA G CUGUGCCU	1754	AGGCACAG GCcgaagGCGaGuCaaGGuCu	UUGGAGGC	9325
1890	UGCCUUGG G UGGCUUUG	1755	CAAAGCCA GCcgaagGCGaGuCaaGGuCu	CCAAGGCA	9326
1893	CUUGGGUG G CUUUGGGG	1756	CCCCAAAG GCcgaagGCGaGuCaaGGuCu	CACCCAAG	9327
1901	GCUUUGGG G CAUGGACA	1757	UGUCCAUG GCcgaagGCGaGuCaaGGuCu	CCCAAAGC	9328
1917	AUUGACCC G UAUAAAGA	1758	UCUUUAUA GCcgaagGCGaGuCaaGGuCu	GGGUCAAU	9329
1933	AAUUUGGA G CUUCUGUG	1759	CACAGAAG GCcgaagGCGaGuCaaGGuCu	UCCAAAUU	9330
1944	UCUGUGGA G UUACUCUC	1760	GAGAGUAA GCcgaagGCGaGuCaaGGuCu	UCCACAGA	9331
2023	AUCGGGGG G CCUUAGAG	1761	CUCUAAGG GCcgaagGCGaGuCaaGGuCu	CCCCGAU	9332
2031	GCCUUAGA G UCUCGGA	1762	UCCGGAGA GCcgaagGCGaGuCaaGGuCu	UCUAAGGC	9333
2062	ACCAUACG G CACUCAGG	1763	CCUGAGUG GCcgaagGCGaGuCaaGGuCu	CGUAUGGU	9334
2070	GCACUCAG G CAAGCUAU	1764	AUAGCUUG GCcgaagGCGaGuCaaGGuCu	CUGAGUGC	9335
2074	UCAGGCAA G CUUUCUG	1765	CAGAAUAG GCcgaagGCGaGuCaaGGuCu	UUGCCUGA	9336
2090	GUGUUGGG G UGAGUUGA	1766	UCAACUCA GCcgaagGCGaGuCaaGGuCu	CCCAACAC	9337
2094	UGGGUGA G UUGAUGAA	1767	UUCAUCAA GCcgaagGCGaGuCaaGGuCu	UCACCCCA	9338
2107	UGAAUCTA G CCACCUGG	1768	CCAGGUGG GCcgaagGCGaGuCaaGGuCu	UAGAUUCA	9339
2116	CCACCUGG G UGGGAAGU	1769	ACUUCCCA GCcgaagGCGaGuCaaGGuCu	CCAGGUGG	9340
2123	GGUGGGAA G UAAUUGG	1770	CCAAAUUA GCcgaagGCGaGuCaaGGuCu	UUCCACC	9341
2140	AAGAUCCA G CAUCCAGG	1771	CCUGGAUG GCcgaagGCGaGuCaaGGuCu	UGGAUCU	9342
2155	GGGAUUA G UAGUCAGC	1772	GCUGACUA GCcgaagGCGaGuCaaGGuCu	UAAUCCC	9343
2158	AAUUAUGA G UCAGCUAU	1773	AUAGCUGA GCcgaagGCGaGuCaaGGuCu	UACUAAU	9344
2162	AGUAGUCA G CUUUGUCA	1774	UGACAUAG GCcgaagGCGaGuCaaGGuCu	UGACUACU	9345
2173	AUGUCAAC G UUAUAUG	1775	CAUAUUA GCcgaagGCGaGuCaaGGuCu	GUUGACAU	9346
2183	UAAUAUGG G CUUAAAA	1776	UUUUUAGG GCcgaagGCGaGuCaaGGuCu	CCAUUUA	9347
2208	CUAUUGUG G UUUCACAU	1777	AUGUGAAA GCcgaagGCGaGuCaaGGuCu	CACAAUAG	9348
2235	ACTUUUGG G CGAGAAAC	1778	GUUUCUCG GCcgaagGCGaGuCaaGGuCu	CCAAAAGU	9349
2260	AAUAUUUG G UGUCUUU	1779	AAAAGACA GCcgaagGCGaGuCaaGGuCu	CAAUAUU	9350
2272	CUUUUGGA G UGUGGAU	1780	AAUCCACA GCcgaagGCGaGuCaaGGuCu	UCCAAAAG	9351
2360	ACGAAGAG G CAGGUCCC	1781	GGGACCUG GCcgaagGCGaGuCaaGGuCu	CUCUUCGU	9352
2364	AGAGGCAG G UCCCCUAG	1782	CUAGGGGA GCcgaagGCGaGuCaaGGuCu	CUGCCUCU	9353
2403	AGACGAAG G UCUCAAUC	1783	GAUUGAGA GCcgaagGCGaGuCaaGGuCu	CUUCGUCU	9354
2417	AUCGCCGC G UCGAGAA	1784	UUCUGCGA GCcgaagGCGaGuCaaGGuCu	GCGGCGAU	9355
2454	CAAUGUUA G UAUCCUU	1785	AAGGAAUA GCcgaagGCGaGuCaaGGuCu	UAACAUUG	9356
2474	CACAUAA G UGGGAAAC	1786	GUUCCCA GCcgaagGCGaGuCaaGGuCu	CUUAUGUG	9357

2491	UUUACGGG G CUUUAUUC	1787	GAAUAAAG GCcgaagGCGaGuCaaGGuCu	CCC GUAAA	9358
2507	CUUCUACG G UACCUUGC	1788	GCAAGGUA GCcgaagGCGaGuCaaGGuCu	CGUAGAAG	9359
2530	CCUAAAUG G CAAACUCC	1789	GGAGUUUG GCcgaagGCGaGuCaaGGuCu	CAUUUAGG	9360
2587	AGAUGUAA G CAAUUUGU	1790	ACAAAUUG GCcgaagGCGaGuCaaGGuCu	UUACAUCU	9361
2599	UUUGUGGG G CCCCUUAC	1791	GUAAGGGG GCcgaagGCGaGuCaaGGuCu	CCCACAAA	9362
2609	CCCUUACA G UAAAUGAA	1792	UUCAUUUA GCcgaagGCGaGuCaaGGuCu	UGUAAGGG	9363
2650	CCUGCUAG G UUUUAUCC	1793	GGAUAAAA GCcgaagGCGaGuCaaGGuCu	CUAGCAGG	9364
2701	AUCAAACC G UAUAUCC	1794	GGAUAAUA GCcgaagGCGaGuCaaGGuCu	GGUUUGAU	9365
2713	UAUCCAGA G UAUGUAGU	1795	ACUACAUA GCcgaagGCGaGuCaaGGuCu	UCUGGAUA	9366
2720	AGUAUGUA G UUAUUAU	1796	AUGAUUAA GCcgaagGCGaGuCaaGGuCu	UACAUACU	9367
2768	UUUGGAAG G CGGGGAUC	1797	GAUCCCCG GCcgaagGCGaGuCaaGGuCu	CUUCCAAA	9368
2791	AAAAGAGA G UCCACACG	1798	CGUGUGGA GCcgaagGCGaGuCaaGGuCu	UCUCUUUU	9369
2799	GUCCACAC G UAGCGCCU	1799	AGGCGCUA GCcgaagGCGaGuCaaGGuCu	GUGUGGAC	9370
2802	CACACGUA G CGCCUAU	1800	AUGAGGCG GCcgaagGCGaGuCaaGGuCu	UACGUGUG	9371
2818	UUUUGCGG G UCACCAUA	1801	UAUGGUGA GCcgaagGCGaGuCaaGGuCu	CCGCAAAA	9372
2848	GAUCUACA G CAUGGGAG	1802	CUCCCAUG GCcgaagGCGaGuCaaGGuCu	UGUAGAUC	9373
2857	CAUGGGAG G UUGGUCUU	1803	AAGACCAA GCcgaagGCGaGuCaaGGuCu	CUCCCAUG	9374
2861	GGAGGUUG G UCUUCCAA	1804	UUGGAAGA GCcgaagGCGaGuCaaGGuCu	CAACCUC	9375
2881	UCGAAAAG G CAUGGGGA	1805	UCCCAUG GCcgaagGCGaGuCaaGGuCu	CUUUUCGA	9376
2936	GAUCAUCA G UUGGACCC	1806	GGGUCCAA GCcgaagGCGaGuCaaGGuCu	UGAUGAUC	9377
2955	CAUUCAAA G CCAACUCA	1807	UGAGUUGG GCcgaagGCGaGuCaaGGuCu	UUUGAAUG	9378
2964	CCAACUCA G UAAAUCCA	1808	UGGAUUUA GCcgaagGCGaGuCaaGGuCu	UGAGUUGG	9379
3005	GACAACUG G CCGGACGC	1809	GCGUCCGG GCcgaagGCGaGuCaaGGuCu	CAGUUGUC	9380
3021	CCAACAAG G UGGGAGUG	1810	CACUCCCA GCcgaagGCGaGuCaaGGuCu	CUUGUUGG	9381
3027	AGGUGGGA G UGGAGCA	1811	UGCUCCCA GCcgaagGCGaGuCaaGGuCu	UCCCACCU	9382
3033	GAGUGGGA G CAUUCGGG	1812	CCCGAAUG GCcgaagGCGaGuCaaGGuCu	UCCCACUC	9383
3041	GCAUUCGG G CCAGGGUU	1813	AACCCUGG GCcgaagGCGaGuCaaGGuCu	CCGAAUGC	9384
3047	GGGCCAGG G UUCACCCC	1814	GGGGUGAA GCcgaagGCGaGuCaaGGuCu	CCUGGCCC	9385
3077	CUGUUGGG G UGGAGCCC	1815	GGGUCCA GCcgaagGCGaGuCaaGGuCu	CCCAACAG	9386
3082	GGGUUGGA G CCCUCACG	1816	CGUGAGGG GCcgaagGCGaGuCaaGGuCu	UCCACCCC	9387
3097	CGCUCAGG G CCUACUCA	1817	UGAGUAGG GCcgaagGCGaGuCaaGGuCu	CCUGAGCG	9388
3117	CUGUGCCA G CAGCUCCU	1818	AGGAGCUG GCcgaagGCGaGuCaaGGuCu	UGGCACAG	9389
3120	UGCCAGCA G CUCCUCCU	1819	AGGAGGAG GCcgaagGCGaGuCaaGGuCu	UGCUGGCA	9390
3146	ACCAAUCG G CAGUCAGG	1820	CCUGACUG GCcgaagGCGaGuCaaGGuCu	CGAUUGGU	9391
3149	AAUCGGCA G UCAGGAAG	1821	CUUCCUGA GCcgaagGCGaGuCaaGGuCu	UGCCGAUU	9392
3158	UCAGGAAG G CAGCCUAC	1822	GUAGGCUG GCcgaagGCGaGuCaaGGuCu	CUUCCUGA	9393
3161	GGAAGGCA G CCUACUCC	1823	GGAGUAGG GCcgaagGCGaGuCaaGGuCu	UGCCUUC	9394
3204	AUCCUCAG G CCAUGCAG	1824	CUGCAUGG GCcgaagGCGaGuCaaGGuCu	CUGAGGAU	9395

Input Sequence = AF100308. Cut Site = YG/M or UG/U.

Stem Length = 8. Core Sequence = GCcgaagGCGaGuCaaGGuCu

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

TABLE IX: HUMAN HBV DNAZYME AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	DNAzyme	Seq ID
508	CAACCAGC A CCGGACCA	833	TGGTCCGG GGCTAGCTACAACGA GCTGGTTG	9396
1632	GAACGCCC A CAGGAACC	1096	GGTTCCGTG GGCTAGCTACAACGA GGGCGTTC	9397
2992	CAACCCGC A CAAGGACA	1376	TGTCCTTG GGCTAGCTACAACGA GCGGGTTG	9398
61	ACUUUCCU G CUGGUGGC	1448	GCCACCAG GGCTAGCTACAACGA AGGAAAGT	9399
94	UGAGCCCU G CUCAGAAU	1450	ATTCTGAG GGCTAGCTACAACGA AGGGCTCA	9400
112	CUGUCUCU G CCAUAUCG	1451	CGATATGG GGCTAGCTACAACGA AGAGACAG	9401
169	AGAACAUC G CAUCAGGA	1454	TCCTGATG GGCTAGCTACAACGA GATGTTCT	9402
192	GGACCCCU G CUCGUGUU	1455	AACACGAG GGCTAGCTACAACGA AGGGGTCC	9403
315	CAAAAUUC G CAGUCCCA	1457	TGGGACTG GGCTAGCTACAACGA GAATTTTG	9404
374	UGGUUAUC G CUGGAUGU	1458	ACATCCAG GGCTAGCTACAACGA GATAACCA	9405
387	AUGUGUCU G CGGCGUUU	1459	AAACGCCG GGCTAGCTACAACGA AGACACAT	9406
410	CUUCCUCU G CAUCCUGC	1460	GCAGGATG GGCTAGCTACAACGA AGAGGAAG	9407
417	UGCAUCCU G CUGCUAUG	1461	CATAGCAG GGCTAGCTACAACGA AGGATGCA	9408
420	AUCCUGCU G CUAUGCCU	1462	AGGCATAG GGCTAGCTACAACGA AGCAGGAT	9409
425	GCUGCUAU G CCUCAUCU	1463	AGATGAGG GGCTAGCTACAACGA ATAGCAGC	9410
468	GGUAUGUU G CCCGUUUG	1464	CAAACGGG GGCTAGCTACAACGA AACATACC	9411
518	CGGACCAU G CAAAACCU	1465	AGGTTTTC GGCTAGCTACAACGA ATGGTCCG	9412
527	CAAAACCU G CACAACUC	1466	GAGTTGTG GGCTAGCTACAACGA AGGTTTTC	9413
538	CAACUCCU G CUCAAGGA	1467	TCCTTGAG GGCTAGCTACAACGA AGGAGTTG	9414
569	CUCAUGUU G CUGUACAA	1468	TTGTACAG GGCTAGCTACAACGA AACATGAG	9415
596	CGGAAACU G CACCUGUA	1469	TACAGGTG GGCTAGCTACAACGA AGTTTCCG	9416
631	GGGCUUUC G CAAAUAUC	1470	GTATTTTC GGCTAGCTACAACGA GAAAGCCC	9417
687	UUACUAGU G CCAUUUGU	1471	ACAAATGG GGCTAGCTACAACGA ACTAGTAA	9418
795	CCCUUUAU G CCGCUGUU	1474	AACAGCGG GGCTAGCTACAACGA ATAAAGGG	9419
798	UUUAUGCC G CUGUUACC	1475	GGTAACAG GGCTAGCTACAACGA GGCATAAA	9420
911	GGCACAUC G CCACAGGA	1476	TCCTGTGG GGCTAGCTACAACGA AATGTGCC	9421
1020	UGGGGUUU G CCGCCCCU	1479	AGGGGCGG GGCTAGCTACAACGA AAACCCCA	9422
1023	GGUUUGCC G CCCCUUUC	1480	GAAAGGGG GGCTAGCTACAACGA GGCAAACC	9423
1034	CCUUUCAC G CAAUGUGG	1481	CCACATTG GGCTAGCTACAACGA GTGAAAGG	9424
1050	GAUAUUCU G CUUUAUUG	1482	CATTAAAG GGCTAGCTACAACGA AGAATATC	9425
1058	GCUUUAU G CCUUUAUA	1483	TATAAAGG GGCTAGCTACAACGA ATTAAAGC	9426
1068	CUUUAUUA G CAUGCAUA	1484	TATGCATG GGCTAGCTACAACGA ATATAAAG	9427
1072	AUAUGCAU G CAUACAAG	1485	CTTGTATG GGCTAGCTACAACGA ATGCATAT	9428
1103	ACUUUCUC G CCAACUUA	1486	TAAGTTGG GGCTAGCTACAACGA GAGAAAGT	9429
1155	ACCCCGUU G CUCGGCAA	1488	TTGCCGAG GGCTAGCTACAACGA AACGGGGT	9430
1177	UGGUCUAU G CCAAGUGU	1489	ACACTTGG GGCTAGCTACAACGA ATAGACCA	9431
1188	AAGUGUUU G CUGACGCA	1490	TGCGTCAG GGCTAGCTACAACGA AAACACTT	9432
1194	UUGCUGAC G CAACCCCC	1492	GGGGGTTG GGCTAGCTACAACGA GTCAGCAA	9433
1234	CCAUCAGC G CAUGCGUG	1493	CACGCATG GGCTAGCTACAACGA GCTGATGG	9434
1238	CAGCGCAU G CGUGGAAC	1494	GTTCCACG GGCTAGCTACAACGA ATGCGCTG	9435
1262	UCUCCUCU G CCGAUCCA	1495	TGGATCGG GGCTAGCTACAACGA AGAGGAGA	9436
1275	UCCAUAAC G CGGAACUC	1497	GAGTTCCG GGCTAGCTACAACGA GGTATGGA	9437
1290	UCCUAGCC G CUUGUUUU	1498	AAAACAAG GGCTAGCTACAACGA GGCTAGGA	9438
1299	CUUGUUUU G CUCGCAGC	1499	GCTGCGAG GGCTAGCTACAACGA AAAACAAG	9439
1303	UUUUGCUC G CAGCAGGU	1500	ACCTGCTG GGCTAGCTACAACGA GAGCAAAA	9440
1349	UCUGUCGU G CUCUCCCG	1502	CGGGAGAG GGCTAGCTACAACGA ACGACAGA	9441
1357	GCUCUCCC G CAAUAUA	1503	TATATTTG GGCTAGCTACAACGA GGGAGAGC	9442

1382	CCAUGGCU G CUAGGCUG	1504	CAGCCTAG GGCTAGCTACAACGA AGCCATGG	9443
1392	UAGGCUGU G CUGCCAAC	1505	GTTGGCAG GGCTAGCTACAACGA ACAGCCTA	9444
1395	GCUGUGCU G CCAACUGG	1506	CCAGTTGG GGCTAGCTACAACGA AGCACAGC	9445
1411	GAUCCUAC G CGGGACGU	1507	ACGTCCCG GGCTAGCTACAACGA GTAGGATC	9446
1442	CCGUCGCG G CUGAAUCC	1508	GGATTCAG GGCTAGCTACAACGA GCCGACGG	9447
1452	UGAAUCCC G CGGACGAC	1510	GTCGTCCG GGCTAGCTACAACGA GGGATTCA	9448
1474	CCGGGGCC G CUUGGGGC	1512	GCCCCAAG GGCTAGCTACAACGA GGCCCCGG	9449
1489	GCUCUACC G CCCGCUUC	1513	GAAGCGGG GGCTAGCTACAACGA GGTAGAGC	9450
1493	UACCGCCC G CUUCUCCG	1514	CGGAGAAG GGCTAGCTACAACGA GGGCGGTA	9451
1501	GCUUCUCC G CCUAUUGU	1515	ACAATAGG GGCTAGCTACAACGA GGAGAAGC	9452
1528	CACGGGGC G CACCUCUC	1517	GAGAGGTG GGCTAGCTACAACGA GCCCGGTG	9453
1542	CUCUUUAC G CGGACUCC	1518	GGAGTCCG GGCTAGCTACAACGA GTAAAGAG	9454
1559	CCGUCUGU G CCUUCUCA	1519	TGAGAAGG GGCTAGCTACAACGA ACAGACGG	9455
1571	UCUCAUCU G CCGGACCG	1520	CGGTCCGG GGCTAGCTACAACGA AGATGAGA	9456
1583	GACCGUGU G CACUUCGC	1521	GCGAAGTG GGCTAGCTACAACGA ACACGGTC	9457
1590	UGCACUUC G CUUCACCU	1522	AGGTGAAG GGCTAGCTACAACGA GAAGTGCA	9458
1601	UCACCUCU G CACGUCGC	1523	GCGACGTG GGCTAGCTACAACGA AGAGGTGA	9459
1608	UGCACGUC G CAUGGAGA	1524	TCTCCATG GGCTAGCTACAACGA GACGTGCA	9460
1628	CCGUGAAC G CCCACAGG	1526	CCTGTGGG GGCTAGCTACAACGA GTTCACGG	9461
1642	AGGAACCU G CCCAAGGU	1527	ACCTTGGG GGCTAGCTACAACGA AGGTTCTT	9462
1654	AAGGUCUU G CAUAAGAG	1528	CTCTTATG GGCTAGCTACAACGA AAGACCTT	9463
1818	AGCACCAU G CAACUUUU	1533	AAAAGTTG GGCTAGCTACAACGA ATGGTGCT	9464
1835	UCACCUCU G CCUAUUA	1534	TGATTAGG GGCTAGCTACAACGA AGAGGTGA	9465
1883	CAAGCUGU G CCUUGGGU	1535	ACCCAAGG GGCTAGCTACAACGA ACAGCTTG	9466
1959	UCUUUUUU G CCUUCUGA	1537	TCAGAAGG GGCTAGCTACAACGA AAAAAAGA	9467
2002	UCGACACC G CCUCUGCU	1541	AGCAGAGG GGCTAGCTACAACGA GGTGTCGA	9468
2008	CCGCCUCU G CUCUGUAU	1542	ATACAGAG GGCTAGCTACAACGA AGAGGCGG	9469
2282	GUGGAUUC G CACUCCUC	1548	GAGGAGTG GGCTAGCTACAACGA GAATCCAC	9470
2293	CUCCUCCU G CAUAUAGA	1549	TCTATATG GGCTAGCTACAACGA AGGAGGAG	9471
2311	CACCAAU G CCCCUAUC	1550	GATAGGGG GGCTAGCTACAACGA ATTTGGTG	9472
2388	ACUCCUC G CCUCGCAG	1552	CTGCGAGG GGCTAGCTACAACGA GAGGGAGT	9473
2393	CUCGCCUC G CAGACGAA	1553	TTCGTCTG GGCTAGCTACAACGA GAGGCGAG	9474
2412	UCUCAUUC G CCGCGUCG	1555	CGACGCGG GGCTAGCTACAACGA GATTGAGA	9475
2415	CAAUCGCC G CGUCGCAG	1556	CTGCGACG GGCTAGCTACAACGA GGCGATTG	9476
2420	GCCGCGUC G CAGAAGAU	1557	ATCTTCTG GGCTAGCTACAACGA GACGCGGC	9477
2514	GGUACCUU G CUUUAUUC	1558	GATTAAAG GGCTAGCTACAACGA AAGGTACC	9478
2560	AUUCAUUU G CAGGAGGA	1560	TCCTCCTG GGCTAGCTACAACGA AAATGAAT	9479
2641	UUAACUUA G CCUGCUAG	1563	CTAGCAGG GGCTAGCTACAACGA ATAGTTAA	9480
2645	CUAUGCCU G CUAGGUUU	1564	AAACCTAG GGCTAGCTACAACGA AGGCATAG	9481
2677	AAAUUUU G CCCUAGA	1565	TCTAAGGG GGCTAGCTACAACGA AAATATTT	9482
2740	UUCAGAC G CGACAUUA	1566	TAATGTCG GGCTAGCTACAACGA GTCTGGAA	9483
2804	CACGUAGC G CCUCAUUU	1568	AAATGAGG GGCTAGCTACAACGA GCTACGTG	9484
2814	CUCAUUUU G CGGGUCAC	1569	GTGACCCG GGCTAGCTACAACGA AAAATGAG	9485
2946	UGGACCCU G CAUUCAAA	1572	TTTGAATG GGCTAGCTACAACGA AGGTCCA	9486
2990	CUCAACCC G CACAAGGA	1573	TCCTTGTG GGCTAGCTACAACGA GGGTTGAG	9487
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3090	GCCCUCAC G CUCAGGGC	1575	GCCCTGAG GGCTAGCTACAACGA GTGAGGGC	9489
3113	ACAACUGU G CCAGCAGC	1576	GCTGCTGG GGCTAGCTACAACGA ACAGTTGT	9490
3132	CUCCUCCU G CCUCCACC	1577	GGTGGAGG GGCTAGCTACAACGA AGGAGGAG	9491
51	AGGGCCCU G UACUUUCC	1578	GGAAAGTA GGCTAGCTACAACGA AGGGCCCT	9492
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219	UUUUUCUU G UUGACAAA	1582	TTTGTCAA GGCTAGCTACAACGA AAGAAAAA	9496
297	ACACCCGU G UGUCUUGG	1583	CCAAGACA GGCTAGCTACAACGA ACGGGTGT	9497
299	ACCCGUGU G UCUUGGCC	1584	GGCCAAGA GGCTAGCTACAACGA ACACGGGT	9498
347	ACCAACCU G UUGUCCUC	1585	GAGGACAA GGCTAGCTACAACGA AGGTTGGT	9499
350	AACCUGUU G UCCUCCAA	1586	TTGGAGGA GGCTAGCTACAACGA AACAGGTT	9500
362	UCCAAUUU G UCCUGGUU	1587	AACCAGGA GGCTAGCTACAACGA AAATTGGA	9501
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383	CUGGAUGU G UCUGCGGC	1589	GCCGCAGA GGCTAGCTACAACGA ACATCCAG	9503
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465	CAAGGUAU G UUGCCCGU	1591	ACGGGCAA GGCTAGCTACAACGA ATACCTTG	9505
476	GCCCGUUU G UCCUCUAA	1592	TTAGAGGA GGCTAGCTACAACGA AAACGGGC	9506
555	ACCUCUAU G UUUCCUC	1593	GAGGGAAA GGCTAGCTACAACGA ATAGAGGT	9507
566	UCCCUCAU G UUGCUGUA	1594	TACAGCAA GGCTAGCTACAACGA ATGAGGGA	9508
572	AUGUUGCU G UACAAAAC	1595	GTTTGTGA GGCTAGCTACAACGA AGCAACAT	9509
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694	UGCCAUUU G UUCAGUGG	1597	CCACTGAA GGCTAGCTACAACGA AAATGGCA	9511
724	CCCCACU G UCUGGCUU	1598	AAGCCAGA GGCTAGCTACAACGA AGTGGGGG	9512
750	UGGAUGAU G UGUUUUUG	1599	CAAAACCA GGCTAGCTACAACGA ATCATCCA	9513
771	CCAAGUCU G UACAACAU	1600	ATGTTGTA GGCTAGCTACAACGA AGACTTGG	9514
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1251	GAACUUUU G UGUCUCCU	1613	AGGAGACA GGCTAGCTACAACGA AAAGGTTT	9527
1253	ACCUUUGU G UCUCUCU	1614	AGAGGAGA GGCTAGCTACAACGA ACAAGGT	9528
1294	AGCCGCUU G UUUUGCUC	1615	GAGCAAAA GGCTAGCTACAACGA AAGCGGCT	9529
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1390	GUAGGCU G UGCUGCCA	1617	TGGCAGCA GGCTAGCTACAACGA AGCCTAGC	9531
1425	CGUCCUUU G UUUACGUC	1618	GACGTAAA GGCTAGCTACAACGA AAAGGACG	9532
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1719	CAAAGACU G UGUGUUUA	1623	TAAACACA GGCTAGCTACAACGA AGTCTTTG	9537
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1723	GACUGUGU G UUUAAUGA	1625	TCATTAAA GGCTAGCTACAACGA ACACAGTC	9539
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1803	AUUGGUGU G UUCACCAG	1629	CTGGTGAA GGCTAGCTACAACGA ACACCAAT	9543
1850	CAUCUCAU G UUCAUGUC	1630	GACATGAA GGCTAGCTACAACGA ATGAGATG	9544

1856	AUGUUCAU G UCCUACUG	1631	CAGTAGGA GGCTAGCTACAACGA ATGAACAT	9545
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1881	UCCAAGCU G UGCCUUGG	1633	CCAAGGCA GGCTAGCTACAACGA AGCTTGGA	9547
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2013	UCUGUCUCU G UAUCGGGG	1635	CCCCGATA GGCTAGCTACAACGA AGAGCAGA	9549
2045	GGAACAUU G UUCACCUC	1636	GAGGTGAA GGCTAGCTACAACGA AATGTTCC	9550
2082	GCUAUUCU G UGUUGGGG	1637	CCCCAACA GGCTAGCTACAACGA AGAATAGC	9551
2084	UAUUCUGU G UUGGGGUG	1638	CACCCCAA GGCTAGCTACAACGA ACAGAATA	9552
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2205	CAACUAU G UGUUUUCA	1640	TGAAACCA GGCTAGCTACAACGA AATAGTTG	9554
2222	CAUUUCCU G UCUUACUU	1641	AAGTAAGA GGCTAGCTACAACGA AGGAAATG	9555
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258	CUAGACUC G UGGUGGAC	1668	GTCCACCA GGCTAGCTACAACGA GAGTCTAG	9582
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461	CUAUCAAG G UAUGUUGC	1678	GCAACATA GGCTAGCTACAACGA CTTGATAG	9592
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625	CAUCUUGG G CUUUCGCA	1681	TGCGAAAG GGCTAGCTACAACGA CCAAGATG	9595

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711	UUCGUAGG G CUUUCCCC	1692	GGGGAAAG GGCTAGCTACAACGA CCTACGAA	9606
729	ACUGUCUG G CUUUCAGU	1693	ACTGAAAG GGCTAGCTACAACGA CAGACAGT	9607
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767	GGGGCCAA G UCUGUACA	1697	TGTACAGA GGCTAGCTACAACGA TTGGCCCC	9611
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1016	CUUUUGGG G UUUGCCGC	1705	GCGGCAAA GGCTAGCTACAACGA CCAAAAAG	9619
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1218	GGGGCUUG G CCAUAGGC	1718	GCCTATGG GGCTAGCTACAACGA CAAGCCCC	9632
1225	GGCCAUAG G CCAUCAGC	1719	GCTGATGG GGCTAGCTACAACGA CTATGGCC	9633
1232	GGCCAUCA G CGCAUGCG	1720	CGCATGCG GGCTAGCTACAACGA TGATGGCC	9634
1240	GCGCAUGC G UGGAACCU	1721	AGGTTCCA GGCTAGCTACAACGA GCATGCGC	9635
1287	AACUCCUA G CCGCUUGU	1722	ACAAGCGG GGCTAGCTACAACGA TAGGAGTT	9636
1306	UGCUCGCA G CAGGUCUG	1723	CAGACCTG GGCTAGCTACAACGA TGCGAGCA	9637
1310	CGCAGCAG G UCUGGGGC	1724	GCCCCAGA GGCTAGCTACAACGA CTGCTGCG	9638
1317	GGUCUGGG G CAAAACUC	1725	GAGTTTTG GGCTAGCTACAACGA CCCAGACC	9639
1347	AUUCUGUC G UGCUCUCC	1726	GGAGAGCA GGCTAGCTACAACGA GACAGAAT	9640
1379	UUUCCAUG G CUGCUAGG	1727	CCTAGCAG GGCTAGCTACAACGA CATGGAAA	9641
1387	GCUCUAG G CUGUGCUG	1728	CAGCACAG GGCTAGCTACAACGA CTAGCAGC	9642
1418	CGCGGGAC G UCCUUUGU	1729	ACAAAGGA GGCTAGCTACAACGA GTCCCGCG	9643
1431	UUGUUUAC G UCCCGUCG	1730	CGACGGGA GGCTAGCTACAACGA GTAAACAA	9644
1436	UACGUCCC G UCGGCGCU	1731	AGCGCCGA GGCTAGCTACAACGA GGGACGTA	9645
1440	UCCCGUCG G CGCUGAAU	1732	ATTCAGCG GGCTAGCTACAACGA CGACGGGA	9646

1471	CUCCCCGG G CCGCUUGG	1733	CCAAGCGG GGCTAGCTACAACGA CCCGGGAG	9647
1481	CGCUUGGG G CUCUACCG	1734	CGGTAGAG GGCTAGCTACAACGA CCCAAGCG	9648
1517	UACCGACC G UCCACGGG	1735	CCCGTGGA GGCTAGCTACAACGA GGTCGGTA	9649
1526	UCCACGGG G CGCACCUC	1736	GAGGTGCG GGCTAGCTACAACGA CCCGTGGA	9650
1553	GACUCCCC G UCUGUGCC	1737	GGCACAGA GGCTAGCTACAACGA GGGGAGTC	9651
1579	GCCGGACC G UGUGCACU	1738	AGTGCACA GGCTAGCTACAACGA GGTCCGGC	9652
1605	CUCUGCAC G UCGCAUGG	1739	CCATGCGA GGCTAGCTACAACGA GTGCAGAG	9653
1622	AGACCACC G UGAACGCC	1740	GGCGTTCA GGCTAGCTACAACGA GGTGGTCT	9654
1649	UGCCCAAG G UCUGCAU	1741	ATGCAAGA GGCTAGCTACAACGA CTGGGGCA	9655
1679	GACUUUCA G CAAUGUCA	1742	TGACATG GGCTAGCTACAACGA TGAAAGTC	9656
1703	ACCUUGAG G CAUACUUC	1743	GAAGTATG GGCTAGCTACAACGA CTCAAGGT	9657
1732	UUUAAUGA G UGGGAGGA	1744	TCCTCCCA GGCTAGCTACAACGA TCATTAAA	9658
1741	UGGGAGGA G UUGGGGGA	1745	TCCCCCAA GGCTAGCTACAACGA TCCTCCCA	9659
1754	GGGAGGAG G UUAGGUUA	1746	TAACCTAA GGCTAGCTACAACGA CTCCTCCC	9660
1759	GAGGUUAG G UUAAAGGU	1747	ACCTTTAA GGCTAGCTACAACGA CTAACCTC	9661
1766	GGUAAAG G UCUUUGUA	1748	TACAAAGA GGCTAGCTACAACGA CTTTAACC	9662
1782	ACUAGGAG G CUGUAGGC	1749	GCCTACAG GGCTAGCTACAACGA CTCCTAGT	9663
1789	GGCUGUAG G CAUAAAUU	1750	AATTTATG GGCTAGCTACAACGA CTACAGCC	9664
1799	AUAAAUUG G UGUGUUCA	1751	TGAACACA GGCTAGCTACAACGA CAATTTAT	9665
1811	GUUACCA G CACCAUGC	1752	GCATGGTG GGCTAGCTACAACGA TGGTGAAC	9666
1870	CUGUCAA G CCUCCAAG	1753	CTTGGAGG GGCTAGCTACAACGA TTGAACAG	9667
1878	GCCUCAA G CUGUGCCU	1754	AGGCACAG GGCTAGCTACAACGA TTGGAGGC	9668
1890	UGCCUUGG G UGGCUUUG	1755	CAAAGCCA GGCTAGCTACAACGA CCAAGGCA	9669
1893	CUUGGGUG G CUUUGGGG	1756	CCCCAAG GGCTAGCTACAACGA CACCCAAG	9670
1901	GCUUUGGG G CAUGGACA	1757	TGTCCATG GGCTAGCTACAACGA CCCAAGC	9671
1917	AUUGACCC G UAUAAGA	1758	TCTTTATA GGCTAGCTACAACGA GGGTCAAT	9672
1933	AAUUUGGA G CUUCUGUG	1759	CACAGAAG GGCTAGCTACAACGA TCCAAATT	9673
1944	UCUGUGGA G UUAUCUC	1760	GAGAGTAA GGCTAGCTACAACGA TCCACAGA	9674
2023	AUCGGGGG G CCUUGAG	1761	CTCTAAGG GGCTAGCTACAACGA CCCCCGAT	9675
2031	GCCUUGA G UCUCGGG	1762	TCCGGAGA GGCTAGCTACAACGA TCTAAGGC	9676
2062	ACCAUACG G CACUCAGG	1763	CCTGAGTG GGCTAGCTACAACGA CGTATGGT	9677
2070	GCACUCAG G CAAGCUAU	1764	ATAGCTTG GGCTAGCTACAACGA CTGAGTGC	9678
2074	UCAGGCAA G CUAUUCUG	1765	CAGAATAG GGCTAGCTACAACGA TTGCCTGA	9679
2090	GUGUUGGG G UGAGUUGA	1766	TCAACTCA GGCTAGCTACAACGA CCCAACAC	9680
2094	UGGGGUGA G UUGAUGAA	1767	TTCATCAA GGCTAGCTACAACGA TCACCCCA	9681
2107	UGAAUCUA G CCACUGG	1768	CCAGGTGG GGCTAGCTACAACGA TAGATTCA	9682
2116	CCACUGG G UGGGAAGU	1769	ACTTCCCA GGCTAGCTACAACGA CCAGGTGG	9683
2123	GGUGGGAA G UAAUUUGG	1770	CCAAATTA GGCTAGCTACAACGA TTCCCACC	9684
2140	AAGAUCCA G CAUCCAGG	1771	CCTGGATG GGCTAGCTACAACGA TGGATCTT	9685
2155	GGGAAUUA G UAGUCAGC	1772	GCTGACTA GGCTAGCTACAACGA TAATTCCC	9686
2158	AAUUAGUA G UCAGCUAU	1773	ATAGCTGA GGCTAGCTACAACGA TACTAATT	9687
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2173	AUGUCAAC G UUAUAUG	1775	CATATTA GGCTAGCTACAACGA GTTGACAT	9689
2183	UAUAUGG G CCUAAAA	1776	TTTTTAGG GGCTAGCTACAACGA CCATATTA	9690
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2260	AAUAUUUG G UGUCUUUU	1779	AAAAGACA GGCTAGCTACAACGA CAAATATT	9693
2272	CUUUUGGA G UGUGGAUU	1780	AATCCACA GGCTAGCTACAACGA TCCAAAG	9694
2360	ACGAAGAG G CAGGUCCC	1781	GGGACCTG GGCTAGCTACAACGA CTCTCGT	9695
2364	AGAGGCAG G UCCCCUAG	1782	CTAGGGGA GGCTAGCTACAACGA CTGCCTCT	9696
2403	AGACGAAG G UCUCAUC	1783	GATTGAGA GGCTAGCTACAACGA CTTCTCT	9697

2417	AUCGCCGC G UCGCAGAA	1784	TTCTGCCA GGCTAGCTACAACGA GCGGCGAT	9698
2454	CAAUGUUA G UAUUCCUU	1785	AAGGAATA GGCTAGCTACAACGA TAACATTG	9699
2474	CACAUAG G UGGGAAAC	1786	GTTTCCCA GGCTAGCTACAACGA CTTATGTG	9700
2491	UUUACGGG G CUUUUUAUC	1787	GAATAAAG GGCTAGCTACAACGA CCCGTAAA	9701
2507	CUUCUACG G UACCUUGC	1788	GCAAGGTA GGCTAGCTACAACGA CGTAGAAG	9702
2530	CCUAAAUG G CAAACUCC	1789	GGAGTTTG GGCTAGCTACAACGA CATTTAGG	9703
2587	AGAUGUAA G CAAUUGU	1790	ACAAATTG GGCTAGCTACAACGA TTACATCT	9704
2599	UUUGUGGG G CCCCUUAC	1791	GTAAGGGG GGCTAGCTACAACGA CCCACAAA	9705
2609	CCCUUACA G UAAAUGAA	1792	TTCATTTA GGCTAGCTACAACGA TGTAAGGG	9706
2650	CCUGCUAG G UUUUAUCC	1793	GGATAAAA GGCTAGCTACAACGA CTAGCAGG	9707
2701	AUCAAACC G UAUUAUCC	1794	GGATAATA GGCTAGCTACAACGA GGTTTGAT	9708
2713	UAUCCAGA G UAUGUAGU	1795	ACTACATA GGCTAGCTACAACGA TCTGGATA	9709
2720	AGUAUGUA G UUAUUAU	1796	ATGATTAA GGCTAGCTACAACGA TACATACT	9710
2768	UUUGGAAG G CGGGGAUC	1797	GATCCCCG GGCTAGCTACAACGA CTTCCAAA	9711
2791	AAAAGAGA G UCCACACG	1798	CGTGTGGA GGCTAGCTACAACGA TCTCTTTT	9712
2799	GUCCACAC G UAGCGCCU	1799	AGGCGCTA GGCTAGCTACAACGA GTGTGGAC	9713
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2857	CAUGGGAG G UUGGUCUU	1803	AAGACCAA GGCTAGCTACAACGA CTCCCATG	9717
2861	GGAGGUUG G UCUUCCAA	1804	TTGGAAGA GGCTAGCTACAACGA CAACCTCC	9718
2881	UCGAAAAG G CAUGGGGA	1805	TCCCATATG GGCTAGCTACAACGA CTTTTTGA	9719
2936	GAUCAUCA G UUGGACCC	1806	GGGTCCAA GGCTAGCTACAACGA TGATGATC	9720
2955	CAUUCAAA G CCAACUCA	1807	TGAGTTGG GGCTAGCTACAACGA TTTGAATG	9721
2964	CCAACUCA G UAAAUCCA	1808	TGGATTTA GGCTAGCTACAACGA TGAGTTGG	9722
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3021	CCAACAAG G UGGGAGUG	1810	CACTCCCA GGCTAGCTACAACGA CTTGTTGG	9724
3027	AGGUGGGA G UGGGAGCA	1811	TGCTCCCA GGCTAGCTACAACGA TCCCACCT	9725
3033	GAGUGGGA G CAUUCGGG	1812	CCCGAATG GGCTAGCTACAACGA TCCCCTC	9726
3041	GCAUUCGG G CCAGGGUU	1813	AACCCTGG GGCTAGCTACAACGA CCGAATGC	9727
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3077	CUGUUGGG G UGGAGCCC	1815	GGGTCCA GGCTAGCTACAACGA CCCAACAG	9729
3082	GGGUGGA G CCCUCACG	1816	CGTGAGGG GGCTAGCTACAACGA TCCACCCC	9730
3097	CGCUCAGG G CCUACUCA	1817	TGAGTAGG GGCTAGCTACAACGA CCTGAGCG	9731
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3120	UGCCAGCA G CUCCUCCU	1819	AGGAGGAG GGCTAGCTACAACGA TGCTGGCA	9733
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3149	AAUCGGCA G UCAGGAAG	1821	CTTCCTGA GGCTAGCTACAACGA TGCCGATT	9735
3158	UCAGGAAG G CAGCCUAC	1822	GTAGGCTG GGCTAGCTACAACGA CTTCTCTGA	9736
3161	GGAAGGCA G CCUACUCC	1823	GGAGTAGG GGCTAGCTACAACGA TGCCCTCC	9737
3204	AUCCUCAG G CCAUGCAG	1824	CTGCATGG GGCTAGCTACAACGA CTGAGGAT	9738
10	ACUCCACC A CUUCCAC	703	GTGGAAAG GGCTAGCTACAACGA GGTGGAGT	9739
17	CACUUUCC A CCAACUC	706	GAGTTTGG GGCTAGCTACAACGA GGAAAGTG	9740
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32	UCUUAAG A UCCAGAG	1826	CTCTGGGA GGCTAGCTACAACGA CTTGAAGA	9742
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82	GUUCAGGA A CAGUGAGC	1827	GCTCACTG GGCTAGCTACAACGA TCCTGAAC	9744
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117	UCUGCCAU A UCGUCAU	53	ATTGACGA GGCTAGCTACAACGA ATGGCAGA	9748

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155	UGUACCGA A CAUGGAGA	1832	TCTCCATG GGCTAGCTACAACGA TCGGTACA	9754
157	UACCGAAC A UGGAGAAC	745	GTTCTCCA GGCTAGCTACAACGA GTTCGGTA	9755
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238	UCCUCACA A UACCACAG	1838	CTGTGGTA GGCTAGCTACAACGA TGTGAGGA	9765
240	CUCACAAU A CCACAGAG	77	CTCTGTGG GGCTAGCTACAACGA ATTGTGAG	9766
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254	GAGUCUAG A CUCGUGGU	1839	ACCACGAG GGCTAGCTACAACGA CTAGACTC	9768
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400	GUUUUAUC A UCUCUCUC	802	GAGGAAGA GGCTAGCTACAACGA GATAAAAC	9782
412	UCCUCUGC A UCCUGCUG	807	CAGCAGGA GGCTAGCTACAACGA GCAGAGGA	9783
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523	CAUGCAAA A CCUGCACA	1854	TGTGCAAG GGCTAGCTACAACGA TTTGCATG	9796
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908	UGGGGCAC A UUGCCACA	924	TGTGGCAA GGCTAGCTACAACGA GTGCCCA	9843
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936	UACAAAAA A UCAAAUUG	1873	CATTTTGA GGCTAGCTACAACGA TTTTGTGA	9849
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1032	CCCCUUUC A CGCAAUGU	944	ACATTGCG GGCTAGCTACAACGA GAAAGGGG	9858
1037	UUCACGCA A UGUGGAUA	1880	TATCCACA GGCTAGCTACAACGA TCGGTGAA	9859
1043	CAAUGUGG A UAUUCUGC	1881	GCAGATAA GGCTAGCTACAACGA CCACATTG	9860
1045	AUGUGGAU A UUCUGCTU	262	AAGCAGAA GGCTAGCTACAACGA ATCCACAT	9861
1056	CUGCUUUA A UGCCUUUA	1882	TAAAGGCA GGCTAGCTACAACGA TAAAGCAG	9862
1064	AUGCCUUU A UAUGCAUG	270	CATGCATA GGCTAGCTACAACGA AAAGGCAT	9863
1066	GCCUUUAU A UGCAUGCA	271	TGCATGCA GGCTAGCTACAACGA ATAAAGGC	9864
1070	UUAUAUGC A UGCAUACA	950	TGTATGCA GGCTAGCTACAACGA GCATATAA	9865
1074	AUGCAUGC A UACAAGCA	951	TGCTTGTA GGCTAGCTACAACGA GCATGCAT	9866
1076	GCAUGCAU A CAAGCAAA	272	TTTGCTTG GGCTAGCTACAACGA ATGCATGC	9867
1085	CAAGCAAA A CAGGCUUU	1883	AAAGCCTG GGCTAGCTACAACGA TTTGCTTG	9868
1095	AGGCUUUU A CUUUCUCG	276	CGAGAAAG GGCTAGCTACAACGA AAAAGCCT	9869
1107	UCUCGCCA A CUUACAAG	1884	CTTGTAAG GGCTAGCTACAACGA TGGCGAGA	9870
1111	GCCAACUU A CAAGCCCU	282	AGGCCTTG GGCTAGCTACAACGA AAGTTGGC	9871
1130	CUAAGUAA A CAGUAUGU	1885	ACATACTG GGCTAGCTACAACGA TTAATTAG	9872
1135	UAAACAGU A UGUGAACC	288	GGTTCACA GGCTAGCTACAACGA ACTGTTTA	9873
1141	GUUUGUGA A CCUUUACC	1886	GGTAAAGG GGCTAGCTACAACGA TCACATAC	9874
1147	GAACCUUU A CCCCUGUG	291	CAACGGGG GGCTAGCTACAACGA AAAGTTTC	9875
1163	GCUCGGCA A CGGCCUGG	1887	CCAGGCCG GGCTAGCTACAACGA TGCCGAGC	9876
1175	CCUGGUCU A UGCCAAGU	295	ACTTGCGA GGCTAGCTACAACGA AGACCAGG	9877
1192	GUUUGCUG A CGCAACCC	1888	GGGTGCGG GGCTAGCTACAACGA CAGCAAAC	9878
1197	CUGACGCA A CCCCACU	1889	AGTGGGGG GGCTAGCTACAACGA TCGCTCAG	9879
1203	CAACCCCC A CUGGUUGG	984	CCAACCAG GGCTAGCTACAACGA GGGGGTTG	9880
1221	GCUUGGCC A UAGGCCAU	988	ATGGCCTA GGCTAGCTACAACGA GGCCAAGC	9881
1228	CAUAGGCC A UCAGCGCA	990	TGCGCTGA GGCTAGCTACAACGA GGCCTATG	9882
1236	AUCAGCGC A UGCGUGGA	992	TCCACGCA GGCTAGCTACAACGA GCGCTGAT	9883
1245	UGCGUGGA A CCUUUGUG	1890	CACAAAGG GGCTAGCTACAACGA TCCACGCA	9884
1266	CUCUGCCG A UCCAUACC	1891	GGTATGGA GGCTAGCTACAACGA CGGCAGAG	9885
1270	GCCGAUCC A UACCGCGG	1001	CCGCGGTA GGCTAGCTACAACGA GGATCGGC	9886
1272	CGAUCCAU A CCGCGGAA	308	TTCCGCGG GGCTAGCTACAACGA ATGGATCG	9887
1280	ACCGCGGA A CUCCUAGC	1892	GCTAGGAG GGCTAGCTACAACGA TCCGCGGT	9888
1322	GGGGCAAA A CUCAUCGG	1893	CCGATGAG GGCTAGCTACAACGA TTTGCCCC	9889
1326	CAAAACUC A UCGGGACU	1014	AGTCCCGA GGCTAGCTACAACGA GAGTTTGT	9890
1332	UCAUCGGG A CUGACAAU	1894	ATTGTCTG GGCTAGCTACAACGA CCCGATGA	9891
1336	CGGGACUG A CAAUUCUG	1895	CAGAATTG GGCTAGCTACAACGA CAGTCCCG	9892
1339	GACUGACA A UUCUGUCG	1896	CGACAGAA GGCTAGCTACAACGA TGTCAGTC	9893
1361	UCCCGCAA A UAUACAUC	1897	GATGTATA GGCTAGCTACAACGA TTGCGGGA	9894
1363	CCGCAAAU A UACAUCAU	324	ATGATGTA GGCTAGCTACAACGA ATTTGCGG	9895
1365	GCAAAUUA A CAUCAUUU	325	AAATGATG GGCTAGCTACAACGA ATATTTCG	9896
1367	AAUAUAC A UCAUUUCC	1023	GGAAATGA GGCTAGCTACAACGA GTATATTT	9897
1370	UAUACAUC A UUUCCAUG	1024	CATGGAAA GGCTAGCTACAACGA GATGTATA	9898
1376	UCAUUUCC A UGGCUGCU	1026	AGCAGCCA GGCTAGCTACAACGA GGAAATGA	9899
1399	UGCUGCCA A CUGGAUCC	1898	GGATCCAG GGCTAGCTACAACGA TGGCAGCA	9900
1404	CCAACUGG A UCCUACGC	1899	GCGTAGGA GGCTAGCTACAACGA CCAGTTGG	9901

1409	UGGAUCCU A CGCGGGAC	332	GTCCCGCG GGCTAGCTACAACGA AGGATCCA	9902
1416	UACGCGGG A CGUCCUUU	1900	AAAGGACG GGCTAGCTACAACGA CCCGCGTA	9903
1429	CUUUGUUU A CGUCCCGU	338	ACGGGACG GGCTAGCTACAACGA AAACAAAG	9904
1447	GGCGCUGA A UCCCGCGG	1901	CCGCGGGA GGCTAGCTACAACGA TCAGCGCC	9905
1456	UCCCGCGG A CGACCCCU	1902	AGGGGTCG GGCTAGCTACAACGA CCGCGGGA	9906
1459	CGCGGACG A CCCCUCCC	1903	GGGAGGGG GGCTAGCTACAACGA CGTCCGCG	9907
1486	GGGGCUCU A CCGCCCGC	345	GCGGGCGG GGCTAGCTACAACGA AGAGCCCC	9908
1505	CUCCGCCU A UUGUACCG	349	CGGTACAA GGCTAGCTACAACGA AGGCGGAG	9909
1510	CCUAUUGU A CCGACCGU	351	ACGGTCGG GGCTAGCTACAACGA ACAATAGG	9910
1514	UUGUACCG A CCGUCCAC	1904	GTGGACGG GGCTAGCTACAACGA CGGTACAA	9911
1521	GACCGUCC A CGGGGCGC	1064	GCGCCCCG GGCTAGCTACAACGA GGACGGTC	9912
1530	CGGGGCGC A CCUCUCUU	1065	AAGAGAGG GGCTAGCTACAACGA GCGCCCCG	9913
1540	CUCUCUUU A CGCGGACU	357	AGTCCGCG GGCTAGCTACAACGA AAAGAGAG	9914
1546	UUACGCGG A CUCCCCGU	1905	ACGGGGAG GGCTAGCTACAACGA CCGCGTAA	9915
1567	GCCUUCUC A UCUGCCGG	1078	CCGGCAGA GGCTAGCTACAACGA GAGAAGGC	9916
1576	UCUGCCGG A CCGUGUGC	1906	GCACACGG GGCTAGCTACAACGA CCGGCAGA	9917
1585	CCGUGUGC A CUUCGCUU	1082	AAGCGAAG GGCTAGCTACAACGA GCACACGG	9918
1595	UUCGCUUC A CCUCUGCA	1085	TGCAGAGG GGCTAGCTACAACGA GAAGCGAA	9919
1603	ACCUCUGC A CGUCGCAU	1089	ATGCGACG GGCTAGCTACAACGA GCAGAGGT	9920
1610	CACGUCGC A UGGAGACC	1090	GGTCTCCA GGCTAGCTACAACGA GCGACGTG	9921
1616	GCAUGGAG A CCACCGUG	1907	CACGGTGG GGCTAGCTACAACGA CTCCATGC	9922
1619	UGGAGACC A CCGUGAAC	1092	GTTCACGG GGCTAGCTACAACGA GGTCTCCA	9923
1626	CACCGUGA A CGCCACA	1908	TGTGGGCG GGCTAGCTACAACGA TCACGGTG	9924
1638	CCACAGGA A CCUGCCCA	1909	TGGGCAGG GGCTAGCTACAACGA TCCTGTGG	9925
1656	GGUCUUGC A UAAGAGGA	1104	TCCTCTTA GGCTAGCTACAACGA GCAAGACC	9926
1664	AUAAGAGG A CUCUUGGA	1910	TCCAAGAG GGCTAGCTACAACGA CCTCTTAT	9927
1672	ACUCUUGG A CUUUCAGC	1911	GCTGAAAG GGCTAGCTACAACGA CCAAGAGT	9928
1682	UUUCAGCA A UGUCAACG	1912	CGTTGACA GGCTAGCTACAACGA TGCTGAAA	9929
1688	CAAUGUCA A CGACCGAC	1913	GTCGGTCG GGCTAGCTACAACGA TGACATTG	9930
1691	UGUCAACG A CCGACCUU	1914	AAGGTCGG GGCTAGCTACAACGA CGTTGACA	9931
1695	AACGACCG A CCUUGAGG	1915	CCTCAAGG GGCTAGCTACAACGA CGGTCGTT	9932
1705	CUUGAGGC A UACUUCAA	1114	TTGAAGTA GGCTAGCTACAACGA GCCTCAAG	9933
1707	UGAGGCAU A CUUCAAG	380	CTTTGAAG GGCTAGCTACAACGA ATGCCTCA	9934
1716	CUUCAAAAG A CUGUGUGU	1916	ACACACAG GGCTAGCTACAACGA CTTTGAAG	9935
1728	UGUGUUUA A UGAGUGGG	1917	CCCACTCA GGCTAGCTACAACGA TAAACACA	9936
1774	GUCUUUGU A CUAGGAGG	394	CCTCCTAG GGCTAGCTACAACGA ACAAGAC	9937
1791	CUGUAGGC A UAAAUUGG	1121	CCAATTTA GGCTAGCTACAACGA GCCTACAG	9938
1795	AGGCAUAA A UUGGUGUG	1918	CACACCAA GGCTAGCTACAACGA TTATGCCT	9939
1807	GUGUGUUC A CCAGCACC	1122	GGTGCTGG GGCTAGCTACAACGA GAACACAC	9940
1813	UCACCAGC A CCAUGCAA	1125	TTGCATGG GGCTAGCTACAACGA GCTGGTGA	9941
1816	CCAGCACC A UGCAACUU	1127	AAGTTGCA GGCTAGCTACAACGA GGTGCTGG	9942
1821	ACCAUGCA A CUUUUUA	1919	TGAAAAAG GGCTAGCTACAACGA TGCAATGG	9943
1829	ACUUUUUC A CCUCUGCC	1130	GGCAGAGG GGCTAGCTACAACGA GAAAAAGT	9944
1840	UCUGCCUA A UCAUCUCA	1920	TGAGATGA GGCTAGCTACAACGA TAGGCAGA	9945
1843	GCCUAAUC A UCUCUUGU	1136	ACATGAGA GGCTAGCTACAACGA GATTAGGC	9946
1848	AUCAUCUC A UGUUCAUG	1138	CATGAACA GGCTAGCTACAACGA GAGATGAT	9947
1854	UCAUGUUC A UGUCCUAC	1139	GTAGGACA GGCTAGCTACAACGA GAACATGA	9948
1861	CAUGUCCU A CUGUUCAA	414	TTGAACAG GGCTAGCTACAACGA AGGACATG	9949
1903	UUUGGGGC A UGGACAUU	1152	AATGTCCA GGCTAGCTACAACGA GCCCCAAA	9950
1907	GGGCAUGG A CAUUGACC	1921	GGTCAATG GGCTAGCTACAACGA CCATGCCC	9951
1909	GCAUGGAC A UUGACCCG	1153	CGGGTCAA GGCTAGCTACAACGA GTCCATGC	9952

1913	GGACAUUG A CCCGUUAU	1922	TATACGGG GGCTAGCTACAACGA CAATGTCC	9953
1919	UGACCCGU A UAAAGAAU	422	ATTCTTTA GGCTAGCTACAACGA ACGGGTCA	9954
1926	UAUAAAGA A UUUGGAGC	1923	GCTCCAAA GGCTAGCTACAACGA TCTTTATA	9955
1947	GUGGAGUU A CUCUCUUU	429	AAAGAGAG GGCTAGCTACAACGA AACTCCAC	9956
1967	GCCUUCUG A CUUCUUUC	1924	GAAAGAAG GGCTAGCTACAACGA CAGAAGGC	9957
1981	UUCCUUCU A UUCGAGAU	446	ATCTCGAA GGCTAGCTACAACGA AGAAGGAA	9958
1988	UAUUCGAG A UCUCUCUG	1925	CGAGGAGA GGCTAGCTACAACGA CTCGAATA	9959
1997	UCUCUCUG A CACCGCCU	1926	AGGCGGTG GGCTAGCTACAACGA CGAGGAGA	9960
1999	UCCUCGAC A CCGCCUCU	1172	AGAGGCGG GGCTAGCTACAACGA GTCGAGGA	9961
2015	UGCUCUGU A UCGGGGGG	454	CCCCCGA GGCTAGCTACAACGA ACAGAGCA	9962
2040	UCUCGGA A CAUUGUUC	1927	GAACAATG GGCTAGCTACAACGA TCCGAGGA	9963
2042	UCCGGAAC A UUGUUCAC	1183	GTGAACAA GGCTAGCTACAACGA GTTCCGGA	9964
2049	CAUUGUUC A CCUCACCA	1184	TGGTGAGG GGCTAGCTACAACGA GAACAATG	9965
2054	UUCACCUC A CCAUACGG	1187	CCGTATGG GGCTAGCTACAACGA GAGGTGAA	9966
2057	ACCUCACC A UACGGCAC	1189	GTGCCGTA GGCTAGCTACAACGA GGTGAGGT	9967
2059	CUCACCAU A CGGCACUC	464	GAGTGCCG GGCTAGCTACAACGA ATGGTGAG	9968
2064	CAUACGGC A CUCAGGCA	1190	TGCGTGAG GGCTAGCTACAACGA GCCGTATG	9969
2077	GGCAAGCU A UUCUGUGU	466	ACACAGAA GGCTAGCTACAACGA AGCTTGCC	9970
2098	GUGAGUUG A UGAUUCUA	1928	TAGATTCA GGCTAGCTACAACGA CAACTCAC	9971
2102	GUUGAUGA A UCUGCCCA	1929	TGGCTAGA GGCTAGCTACAACGA TCATCAAC	9972
2110	AUCUAGCC A CCUGGGUG	1198	CACCCAGG GGCTAGCTACAACGA GGCTAGAT	9973
2126	GGGAAGUA A UUUGGAAG	1930	CTTCCAAA GGCTAGCTACAACGA TACTTCCC	9974
2135	UUUGGAAG A UCCAGCAU	1931	ATGTGGA GGCTAGCTACAACGA CTTCCAAA	9975
2142	GAUCCAGC A UCCAGGGA	1203	TCCCTGGA GGCTAGCTACAACGA GCTGGATC	9976
2151	UCCAGGGA A UUAGUAGU	1932	ACTACTAA GGCTAGCTACAACGA TCCCTGGA	9977
2165	AGUCAGCU A UGUCAACG	482	CGTTGACA GGCTAGCTACAACGA AGCTGACT	9978
2171	CUAUGUCA A CGUUAUAU	1933	TATTAACG GGCTAGCTACAACGA TGACATAG	9979
2177	CAACGUUA A UAUGGGCC	1934	GGCCATA GGCTAGCTACAACGA TAACGTTG	9980
2179	ACGUUAAU A UGGGCCUA	486	TAGGCCCA GGCTAGCTACAACGA ATTAACGT	9981
2191	GCCUAAAA A UCAGACAA	1935	TTGTCTGA GGCTAGCTACAACGA TTTTAGGC	9982
2196	AAAAUCAG A CAACUAUU	1936	AATAGTTG GGCTAGCTACAACGA CTGATTTT	9983
2199	AUCAGACA A CUUUGUG	1937	CACAATAG GGCTAGCTACAACGA TGTCTGAT	9984
2202	AGACAACU A UUGUGGUU	489	AACCACAA GGCTAGCTACAACGA AGTTGTCT	9985
2213	GUGGUUUC A CAUUUCCU	1214	AGGAAATG GGCTAGCTACAACGA GAAACCAC	9986
2215	GGUUUCAC A UUUCUGU	1215	ACAGGAAA GGCTAGCTACAACGA GTGAAACC	9987
2227	CCUGUCUU A CUUUUGGG	499	CCCAAAAG GGCTAGCTACAACGA AAGACAGG	9988
2242	GGCGAGAA A CUGUUCUU	1938	AAGAACAG GGCTAGCTACAACGA TTCTCGCC	9989
2253	GUUCUUGA A UAUUUGGU	1939	ACCAAATA GGCTAGCTACAACGA TCAAGAAC	9990
2255	UCUUGAAU A UUUGGUGU	506	ACACCAAA GGCTAGCTACAACGA ATTCAAGA	9991
2278	GAGUGUGG A UUCGCACU	1940	AGTGCGAA GGCTAGCTACAACGA CCACACTC	9992
2284	GGAUUCGC A CUCCUCCU	1223	AGGAGGAG GGCTAGCTACAACGA GCGAATCC	9993
2295	CCUCCUGC A UAUAGACC	1229	GGTCTATA GGCTAGCTACAACGA GCAGGAGG	9994
2297	UCCUGCAU A UAGACCAC	517	GTGGTCTA GGCTAGCTACAACGA ATGCAGGA	9995
2301	GCAUUAUAG A CCACCAAA	1941	TTTGGTGG GGCTAGCTACAACGA CTATATGC	9996
2304	UAUAGACC A CCAAUUGC	1231	GCATTTGG GGCTAGCTACAACGA GGTCTATA	9997
2309	ACCACCAA A UGCCCCUA	1942	TAGGGGCA GGCTAGCTACAACGA TTGGTGGT	9998
2317	AUGCCCCU A UCUAUCA	519	TGATAAGA GGCTAGCTACAACGA AGGGGCAT	9999
2322	CCUAUCUU A UCAACACU	522	AGTGTGGA GGCTAGCTACAACGA AAGATAGG	10000
2326	UCUAUCA A CACUCCCG	1943	CGGAAGTG GGCTAGCTACAACGA TGATAAGA	10001
2328	UUAUCAAC A CUUCCGGA	1240	TCCGGAAG GGCTAGCTACAACGA GTTGATAA	10002
2338	UUCCGGAA A CUACUGUU	1944	AACAGTAG GGCTAGCTACAACGA TTCCGGAA	10003

2341	CGGAAACU A CUGUUGUU	526	AACAACAG GGCTAGCTACAACGA AGTTTCCG	10004
2352	GUUGUUAG A CGAAGAGG	1945	CCTCTTCG GGCTAGCTACAACGA CTAACAAC	10005
2380	GAAGAAGA A CUCCCUCG	1946	CGAGGGAG GGCTAGCTACAACGA TCTTCTTC	10006
2397	CCUCGCAG A CGAAGGUC	1947	GACCTTCG GGCTAGCTACAACGA CTGCGAGG	10007
2409	AGGUCUCA A UCGCCGCG	1948	CGCGGCGA GGCTAGCTACAACGA TGAGACCT	10008
2427	CGCAGAAG A UCUCAAUC	1949	GATTGAGA GGCTAGCTACAACGA CTTCTGCG	10009
2433	AGAUCUCA A UCUCGGGA	1950	TCCCGAGA GGCTAGCTACAACGA TGAGATCT	10010
2442	UCUCGGGA A UCUCAAUG	1951	CATTGAGA GGCTAGCTACAACGA TCCCGAGA	10011
2448	GAAUCUCA A UGUUAGUA	1952	TACTAACA GGCTAGCTACAACGA TGAGATTC	10012
2456	AUGUUAGU A UUCCUUGG	547	CCAAGGAA GGCTAGCTACAACGA ACTAACAT	10013
2465	UUCCUUGG A CACAUUAG	1953	CTTATGTG GGCTAGCTACAACGA CCAAGGAA	10014
2467	CCUUGGAC A CAUAAGGU	1268	ACCTTATG GGCTAGCTACAACGA GTCCAAGG	10015
2469	UUGGACAC A UAAGGUGG	1269	CCACCTTA GGCTAGCTACAACGA GTGTCCAA	10016
2481	GGUGGGAA A CUUUACGG	1954	CCGTAAAG GGCTAGCTACAACGA TTCCACC	10017
2486	GAAACUUU A CGGGGCUU	554	AAGCCCCG GGCTAGCTACAACGA AAAGTTTC	10018
2496	GGGGCUUU A UUCUUCUA	557	TAGAAGAA GGCTAGCTACAACGA AAAGCCCC	10019
2504	AUUCUUCU A CGGUACCU	562	AGGTACCG GGCTAGCTACAACGA AGAAGAAT	10020
2509	UCUACGGU A CCUUGCUU	563	AAGCAAGG GGCTAGCTACAACGA ACCGTAGA	10021
2520	UUGCUUUA A UCCUAAAU	1955	ATTTAGGA GGCTAGCTACAACGA TAAAGCAA	10022
2527	AAUCCUAA A UGGCAAAC	1956	GTTTGCCA GGCTAGCTACAACGA TTAGGATT	10023
2534	AAUGGCAA A CUCCUUCU	1957	AGAAGGAG GGCTAGCTACAACGA TTGCCATT	10024
2550	UUUCCUG A CAUUCAUU	1958	AATGAATG GGCTAGCTACAACGA CAGGAAAA	10025
2552	UUCUGAC A UUCAUUG	1286	CAAATGAA GGCTAGCTACAACGA GTCAGGAA	10026
2556	UGACAUUC A UUUGCAGG	1287	CCTGCAAA GGCTAGCTACAACGA GAATGTCA	10027
2568	GCAGGAGG A CAUUGUUG	1959	CAACAATG GGCTAGCTACAACGA CCTCCTGC	10028
2570	AGGAGGAC A UUGUUGAU	1289	ATCAACAA GGCTAGCTACAACGA GTCCTCCT	10029
2577	CAUUGUUG A UAGAUGUA	1960	TACATCTA GGCTAGCTACAACGA CAACAATG	10030
2581	GUUGAUAG A UGUUAGCA	1961	TGCTTACA GGCTAGCTACAACGA CTATCAAC	10031
2590	UGUAGCA A UUUGUGGG	1962	CCCACAAA GGCTAGCTACAACGA TGCTTACA	10032
2606	GGCCCCUU A CAGUAAAU	588	ATTTACTG GGCTAGCTACAACGA AAGGGGCC	10033
2613	UACAGUAA A UGAAAACA	1963	TGTTTTCA GGCTAGCTACAACGA TTAGTGTA	10034
2619	AAAUGAAA A CAGGAGAC	1964	GTCTCCTG GGCTAGCTACAACGA TTTCAATT	10035
2626	AACAGGAG A CUUAAAUU	1965	AATTTAAG GGCTAGCTACAACGA CTCCTGTT	10036
2632	AGACUUA A UUAACUUA	1966	ATAGTTAA GGCTAGCTACAACGA TTAAGTCT	10037
2636	UUAAAUUA A CUAUGCCU	1967	AGGCATAG GGCTAGCTACAACGA TAATTTAA	10038
2639	AAUUAACU A UGCCUGCU	594	AGCAGGCA GGCTAGCTACAACGA AGTTAATT	10039
2655	UAGGUUUU A UCCCAAUG	599	CATTGGGA GGCTAGCTACAACGA AAAACCTA	10040
2661	UUAUCCCA A UGUUACUA	1968	TAGTAACA GGCTAGCTACAACGA TGGGATAA	10041
2666	CCAAUGUU A CUAAAUUA	602	ATATTTAG GGCTAGCTACAACGA AACATTGG	10042
2671	GUUACUAA A UAUUUGCC	1969	GGCAAATA GGCTAGCTACAACGA TTAGTAAC	10043
2673	UACUAAAU A UUUGCCCU	604	AGGGCAAA GGCTAGCTACAACGA ATTTAGTA	10044
2685	GCCCUUAG A UAAAGGGA	1970	TCCCTTTA GGCTAGCTACAACGA CTAAGGGC	10045
2693	AUAAAGGG A UCAAACCG	1971	CGGTTTGA GGCTAGCTACAACGA CCCTTTAT	10046
2698	GGGAUCAA A CCGUAUUA	1972	TAATACGG GGCTAGCTACAACGA TTGATCCC	10047
2703	CAAACCGU A UUAUCCAG	611	CTGGATAA GGCTAGCTACAACGA ACGGTTTG	10048
2706	ACCGUAUU A UCCAGAGU	613	ACTCTGGA GGCTAGCTACAACGA AATACGGT	10049
2715	UCCAGAGU A UGUAGUUA	615	TAACTACA GGCTAGCTACAACGA ACTCTGGA	10050
2724	UGUAGUUA A UCAUUAU	1973	AGTAATGA GGCTAGCTACAACGA TAACTACA	10051
2727	AGUUAUUC A UUAUUCU	1313	GGAAGTAA GGCTAGCTACAACGA GATTAACT	10052
2730	UAAUCAUU A CUUCCAGA	621	TCTGGAAG GGCTAGCTACAACGA AATGATTA	10053
2738	ACUUCAG A CGCGACAU	1974	ATGTCGCG GGCTAGCTACAACGA CTGGAAGT	10054

2743	CAGACGCG A CAUUAUUU	1975	AAATAATG GGCTAGCTACAACGA CGCGTCTG	10055
2745	GACGCGAC A UUAUUUAC	1317	GTAAATAA GGCTAGCTACAACGA GTCGCGTC	10056
2748	GCGACAUU A UUUACACA	625	TGTGTAAA GGCTAGCTACAACGA AATGTGCG	10057
2752	CAUUAUUU A CACACUCU	628	AGAGTGTG GGCTAGCTACAACGA AAATAATG	10058
2754	UUAUUUAC A CACUCUUU	1318	AAAGAGTG GGCTAGCTACAACGA GTAAATAA	10059
2756	AUUUACAC A CUCUUUGG	1319	CCAAAGAG GGCTAGCTACAACGA GTGTAAAT	10060
2774	AGGCGGGG A UCUAUAU	1976	ATATAAGA GGCTAGCTACAACGA CCCC GCCT	10061
2779	GGGAUCUU A UAUAAAAG	634	CTTTTATA GGCTAGCTACAACGA AAGATCCC	10062
2781	GAUCUUAU A UAAAAGAG	635	CTCTTTTA GGCTAGCTACAACGA ATAAGATC	10063
2795	GAGAGUCC A CACGUAGC	1324	GCTACGTG GGCTAGCTACAACGA GGACTCTC	10064
2797	GAGUCCAC A CGUAGCGC	1325	GCGCTACG GGCTAGCTACAACGA GTGGACTC	10065
2809	AGCGCCUC A UUUUGCGG	1328	CCGCAAAA GGCTAGCTACAACGA GAGGCGCT	10066
2821	UGCGGGUC A CCAUAUUC	1329	GAATATGG GGCTAGCTACAACGA GACCCGCA	10067
2824	GGGUCACC A UAUUCUUG	1331	CAAGAATA GGCTAGCTACAACGA GGTGACCC	10068
2826	GUCACCAU A UUCUUGGG	644	CCCAAGAA GGCTAGCTACAACGA ATGGTGAC	10069
2836	UCUUGGGA A CAAGAUCU	1977	AGATCTTG GGCTAGCTACAACGA TCCCAAGA	10070
2841	GGAACAAG A UCUCAGC	1978	GCTGTAGA GGCTAGCTACAACGA CTTGTTC	10071
2845	CAAGAUCU A CAGCAUGG	649	CCATGCTG GGCTAGCTACAACGA AGATCTTG	10072
2850	UCUCAGC A UGGGAGGU	1336	ACCTCCCA GGCTAGCTACAACGA GCTGTAGA	10073
2870	UCUCCAA A CCUCGAAA	1979	TTTCGAGG GGCTAGCTACAACGA TTGGAAGA	10074
2883	GAAAAGGC A UGGGGACA	1342	TGTCCTCA GGCTAGCTACAACGA GCCTTTTC	10075
2889	GCAUGGGG A CAAUCUU	1980	AAGATTG GGCTAGCTACAACGA CCCCATGC	10076
2893	GGGGACAA A UCUCUCUG	1981	CAGAAAGA GGCTAGCTACAACGA TTGTCCCC	10077
2908	UGUCCCCA A UCCCCUGG	1982	CCAGGGGA GGCTAGCTACAACGA TGGGGACA	10078
2918	CCCCUGGG A UUCUCCC	1983	GGGAAGAA GGCTAGCTACAACGA CCCAGGGG	10079
2929	CUUCCCCG A UCAUCAGU	1984	ACTGATGA GGCTAGCTACAACGA CGGGGAAG	10080
2932	CCCCGAUC A UCAGUUGG	1358	CCAACTGA GGCTAGCTACAACGA GATCGGGG	10081
2941	UCAGUUGG A CCCUGCAU	1985	ATGCAGGG GGCTAGCTACAACGA CCAACTGA	10082
2948	GACCCUGC A UUCAAGC	1363	GCTTTGAA GGCTAGCTACAACGA GCAGGGTC	10083
2959	CAAAGCCA A CUCAGUAA	1986	TTACTGAG GGCTAGCTACAACGA TGGCTTTG	10084
2968	CUCAGUAA A UCCAGAUU	1987	AATCTGGA GGCTAGCTACAACGA TTA CTGAG	10085
2974	AAAUCCAG A UUGGGACC	1988	GGTCCCAA GGCTAGCTACAACGA CTGGATTT	10086
2980	AGAUUGGG A CCUCAACC	1989	GGTGTAGG GGCTAGCTACAACGA CCCAATCT	10087
2986	GGACCUCA A CCCGCACA	1990	TGTGCGGG GGCTAGCTACAACGA TGAGGTCC	10088
2998	GCACAAGG A CAACUGGC	1991	GCCAGTTG GGCTAGCTACAACGA CCTTGTGC	10089
3001	CAAGGACA A CUGGCCGG	1992	CCGGCCAG GGCTAGCTACAACGA TGTCTTTG	10090
3010	CUGGCCGG A CGCCAACA	1993	TGTGTGGC GGCTAGCTACAACGA CCGGCCAG	10091
3016	GGACGCCA A CAAGGUGG	1994	CCACCTTG GGCTAGCTACAACGA TGGCGTCC	10092
3035	GUGGGAGC A UUCGGGCC	1384	GGCCCGAA GGCTAGCTACAACGA GCTCCAC	10093
3051	CAGGGUUC A CCCUCCC	1387	GGGAGGGG GGCTAGCTACAACGA GAACCCTG	10094
3061	CCCUCCCC A UGGGGGAC	1395	GTCCCCCA GGCTAGCTACAACGA GGGGAGGG	10095
3068	CAUGGGGG A CUGUUGGG	1995	CCCAACAG GGCTAGCTACAACGA CCCCATG	10096
3088	GAGCCUC A CGUCAGG	1400	CCTGAGCG GGCTAGCTACAACGA GAGGGCTC	10097
3101	CAGGGCCU A CUCACAAC	683	GTTGTGAG GGCTAGCTACAACGA AGGCCCTG	10098
3105	GCCUACUC A CAACUGUG	1406	CACAGTTG GGCTAGCTACAACGA GAGTAGGC	10099
3108	UACUCACA A CUGUGCCA	1996	TGGCACAG GGCTAGCTACAACGA TGTGAGTA	10100
3138	CUGCCUCC A CCAUCGG	1422	CCGATTGG GGCTAGCTACAACGA GGAGGCAG	10101
3142	CUCCACCA A UCGGCAGU	1997	ACTGCCGA GGCTAGCTACAACGA TGGTGGAG	10102
3165	GGCAGCCU A CUCCCUUA	691	TAAGGGAG GGCTAGCTACAACGA AGGCTGCC	10103
3173	ACUCCCUU A UCUCACC	694	GGTGGAGA GGCTAGCTACAACGA AAGGGAGT	10104
3179	UUAUCUCC A CCUCUAAG	1436	CTTAGAGG GGCTAGCTACAACGA GGAGATAA	10105

3190	UCUAAGGG A CACUCAUC	1998	GATGAGTG GGCTAGCTACAACGA CCCTTAGA	10106
3192	UAAGGGAC A CUCAUCCU	1440	AGGATGAG GGCTAGCTACAACGA GTCCCTTA	10107
3196	GGACACUC A UCCUCAGG	1442	CCTGAGGA GGCTAGCTACAACGA GAGTGTCC	10108
3207	CUCAGGCC A UGCAGUGG	1447	CCACTGCA GGCTAGCTACAACGA GGCCTGAG	10109

Input Sequence = AF100308. Cut Site = YG/M or UG/U.

Stem Length = 8 . Core Sequence = GGCTAGCTACAACGA

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

TABLE X: HUMAN HBV AMBERZYME AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	Amberzyme	Seq ID
61	ACUUUCCU G CUGGUGGC	1448	GCCACCAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGGAAAGU	10110
87	GGAAACAGU G AGCCUGGC	1449	GCAGGGCU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG ACUGUUCC	10111
94	UGAGCCCU G CUCAGAAU	1450	AUUCUGAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGGGCUCA	10112
112	CUGUCUCU G CCAUAUCG	1451	CGAUAUGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGAGACAG	10113
132	AUCUUAUC G AGACUGG	1452	CCAGUCUU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GAUAAGAU	10114
153	CCUGUACC G AACAUGGA	1453	UCCAUGUU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGUACAGG	10115
169	AGAACAU G CAUCAGGA	1454	UCCUGAUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GAUGUUCU	10116
192	GGACCCCU G CUCGUGUU	1455	AACACGAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGGGUCC	10117
222	UUCUUGUU G ACAAUAU	1456	AUUUUUGU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AACAGAA	10118
315	CAAAUAUC G CAGUCCCA	1457	UGGACUUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GAUUUUUG	10119
374	UGGUUAUC G CUGGAUGU	1458	ACAUCCAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GAUAACCA	10120
387	AUGUGUCU G CGGCGUUU	1459	AAACGCCG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGACACAU	10121
410	CUUCUCU G CAUCCUGC	1460	GCAGGAUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGAGGAAG	10122
417	UGCAUCCU G CUGCUAUG	1461	CAUAGCAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGGAUGCA	10123
420	AUCCUGCU G CUAUGCCU	1462	AGGCAUAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGCAGGAU	10124
425	GCUGCUAU G CCUCAUCU	1463	AGAUGAGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AUAGCAGC	10125
468	GGUAUGUU G CCGGUUUG	1464	CAAAACGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AACAUACC	10126
518	CGGACCAU G CAAAACCU	1465	AGGUUUUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AUGGUCCG	10127
527	CAAAACCU G CACAACUC	1466	GAGUTUGU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGGUUUUG	10128
538	CAACUCCU G CUCAGGA	1467	UCCUUGAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGGAGUUG	10129
569	CUCAUGUU G CUGUACAA	1468	UUGUACAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AACAUAGAG	10130
596	CGGAAACU G CACCUGUA	1469	UACAGGUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGUUUCCG	10131
631	GGCUUUC G CAAAUAUC	1470	GUUUUUUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GAAAGCCC	10132
687	UUACUAGU G CCAUUUGU	1471	ACAAAUGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG ACUAGUAA	10133
747	AUAUGGAU G AUGUGGUU	1472	AACCACAU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AUCCAUAU	10134
783	AACAUCUU G AGUCCCUU	1473	AAGGGACU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGAUGUUU	10135
795	CCCUUUAU G CCGCUGUU	1474	AACAGCCG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AUAAAGGG	10136
798	UUUAUGCC G CUGUUACC	1475	GGUAACAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGCAUAAA	10137
911	GGCACAUU G CCACAGGA	1476	UCCUGUGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AAUGUGCC	10138
978	GGCCUAUU G AUUGGAAA	1477	UUUCCAAU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AAUAGGCC	10139
997	AUGUCAAC G AAUUGUGG	1478	CCACAAUU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GUUGACAU	10140
1020	UGGGGUUU G CCGCCCUU	1479	AGGGCGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AAACCCCA	10141
1023	GGUUUGCC G CCCUUUUC	1480	GAAAGGGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGCAAACC	10142

1034	CCUUCAC G CAUUGUGG	1481	CCACAUUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUGAAAGG	10143
1050	GAUAUCU G CUUUAUUG	1482	CAUUAAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGAAUUC	10144
1058	GCUUAAU G CCUUUAUA	1483	UAUAAAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUUAAAGC	10145
1068	CUUUAUAU G CAUGCAUA	1484	UAUGCAUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUUAAAG	10146
1072	AUAUGCAU G CAUACAAG	1485	CUUGAUUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUGCAUAU	10147
1103	ACUUCUC G CCAACUUA	1486	UAAGUUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GAGAAAGU	10148
1139	CAGUAUGU G AACUUUA	1487	UAAGGUU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG ACAUACUG	10149
1155	ACCCGUU G CUCGGCA	1488	UUGCCGAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AACGGGU	10150
1177	UGGUCUAU G CCAAGUGU	1489	ACACUUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUAGACCA	10151
1188	AAGUGUUU G CUGACGCA	1490	UGCGUCAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AAACACUU	10152
1191	UGUUGCU G ACGCAACC	1491	GGUUGCU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGCAACAA	10153
1194	UUGCUGAC G CAACCCCC	1492	GGGGUUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUCAGCAA	10154
1234	CCAUCAGC G CAUGCGUG	1493	CACGCAUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GCUGAUGG	10155
1238	CAGCGCAU G CGUGGAAC	1494	GUUCCAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUGCGCUG	10156
1262	UCUCCUCU G CCGAUCCA	1495	UGGAUCGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGAGGAGA	10157
1265	CCUCUGCC G AUCCAUAU	1496	GUUGGAU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGCAGAGG	10158
1275	UCCAUAAC G CGGAACUC	1497	GGAUCCG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGUUGGA	10159
1290	UCCUAGCC G CUUGUUUU	1498	AAAACAAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGCUAGGA	10160
1299	CUUGUUUU G CUCGCAGC	1499	GCUGCGAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AAAACAAG	10161
1303	UUUUGCUC G CAGCAGGU	1500	ACCUGCUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GAGCAAAA	10162
1335	UCGGGACU G ACAAUUCU	1501	AGAAUUGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGUCCCGA	10163
1349	UCUGUCGU G CUCUCCCG	1502	CGGGAGAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG ACACACAA	10164
1357	GCUCUCCC G CAAAUUAU	1503	UAUAUUUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGGAGAGC	10165
1382	CCAUGGCU G CUAGGCGU	1504	CAGCCUAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGCCAUGG	10166
1392	UAGGCGU G CUGCCAAC	1505	GUUGGCAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG ACAGCCUA	10167
1395	GCUGUGCU G CCAACUGG	1506	CCAGUUGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGCACAGC	10168
1411	GAUCCUAC G CGGACGU	1507	ACGUCCCG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUAGGAUC	10169
1442	CCGUCGGC G CUGAAUCC	1508	GGAUUCAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GCCGACGG	10170
1445	UCGGGCGU G AAUCCCGC	1509	GCGGGAU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGCGCCGA	10171
1452	UGAAUCCC G CGGACGAC	1510	GUCGUCCG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGAUUAUA	10172
1458	CCGGGGAC G ACCCUCC	1511	GGAGGGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUCCCGGG	10173
1474	CCGGGGCC G CUJGGGGC	1512	GCCTCAAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGCCCGCG	10174
1489	GCUCUACC G CCCGCUUC	1513	GAAGCGGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGUAGAGC	10175
1493	UACCGCCC G CUUCUCGG	1514	CGGAGAAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGGCGGUA	10176
1501	GCUCUCC G CCUAUUGU	1515	ACAAUAGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGAGAAGC	10177
1513	AUUGUACC G ACCGUCCA	1516	UGGACGGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGUACAAU	10178
1528	CACGGGC G CACCUCUC	1517	GAGAGGUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GCCCGGUG	10179

1542	CUCUUUAC G CGGACUCC	1518	GGAGUCCG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUAAAGAG	10180
1559	CCGUCUGU G CCUUCUCA	1519	UGAGAAGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG ACAGACGG	10181
1571	UCUCAUCU G CCGGACCG	1520	CGGUCCGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGAUGAGA	10182
1583	GACCGUGU G CACUUCGC	1521	GCAGAAGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG ACACGGUC	10183
1590	UGCACUUC G CUUACACU	1522	AGUGAAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GAAGUGCA	10184
1601	UCACCUCU G CACGUCCG	1523	GCACGUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGAGGUGA	10185
1608	UGCACGUC G CAUGGAGA	1524	UCUCAUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GACGUGCA	10186
1624	ACCACCGU G AACGCCCA	1525	UGGCGUUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG ACGGUGGU	10187
1628	CCGUGAAC G CCCACAGG	1526	CCUGUGGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUUCACGG	10188
1642	AGGAACCU G CCCAAGGU	1527	ACCUUGGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGGUUCCU	10189
1654	AAGGUCUU G CAUAAGAG	1528	CUCUUAUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AAGACCUU	10190
1690	AUGUCAAC G ACCGACCU	1529	AGGUCGGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUUGACAU	10191
1694	CAACGACC G ACCUUGAG	1530	CUCAAAGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGUCGUUG	10192
1700	CCGACCUU G AGGCAUAC	1531	GUUGCCU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AAGGUCGG	10193
1730	UGUUUAU G AGUGGGAG	1532	CUCCACU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUUAAACA	10194
1818	AGCACCAU G CAACUUUU	1533	AAAGUUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUGGUGCU	10195
1835	UCACCUCU G CCUAUUA	1534	UGAUUAGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGAGGUGA	10196
1883	CAAGCUGU G CCUUGGGU	1535	ACCAAGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG ACAGCUUG	10197
1912	UGGACAUU G ACCCGUAU	1536	AUAGGGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AAUGUCCA	10198
1959	UCUUUUU G CCUUCUGA	1537	UCAGAAGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AAAAAAGA	10199
1966	UGCCUUCU G ACUUCUUU	1538	AAAGAAGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGAAGGCA	10200
1985	UUCUAUUC G AGAUCUCC	1539	GGAGAUU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GAUAGAA	10201
1996	AUCUCCUC G ACACCGCC	1540	GGCGGUGU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GAGGAGAU	10202
2002	UGACACCC G CCUCUGCU	1541	AGCAGAGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GGUGUCGA	10203
2008	CCGCCUUC G CUCUGUAU	1542	AUACAGAG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGAGGCGG	10204
2092	GUUGGGGU G AGUUGAUG	1543	CAUCAACU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG ACCCCAAC	10205
2097	GGUGAGUU G AUGAAUCU	1544	AGAUUCAU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AACUCACC	10206
2100	GAGUUGAU G AAUCUAGC	1545	GCUAGAUA GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUCAACUC	10207
2237	UUUUGGGC G AGAAACUG	1546	CAGUUUCU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GCCCAAAA	10208
2251	CUGUUCUU G AAUAUUUG	1547	CAAAUAUU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AAGAACAG	10209
2282	GUGGAUUC G CACUCCUC	1548	GAGGAGUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GAUCCAC	10210
2293	CUCCUCCU G CAUAUAGA	1549	UCUAUAUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AGGAGGAG	10211
2311	CACCAAU G CCCCUAUC	1550	GAUAGGGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG AUTUUGUG	10212
2354	UGUAAGAC G AAGAGGCA	1551	UGCCUUCU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUCUAAACA	10213
2388	ACUCCUUC G CCUCGAG	1552	CUGCGAGG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GAGGAGU	10214
2393	CUCGCCUC G CAGACGAA	1553	UUCGUCUG GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GAGGCGAG	10215
2399	UCGCAGAC G AAGGUCUC	1554	GAGACCUU GGAGGAAACUCC CU UCAAGGACAUUGUCCGG GUCUGCGA	10216

2412	UCUCAUC G CCGGUCG	1555	CGACGCG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GAUUGAGA	10217
2415	CAUUGCC G CGUGCAG	1556	CUGCGAC GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GGCGAUUG	10218
2420	GCCGGUC G CAGAAGAU	1557	AUCUUCG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GACGCGC	10219
2514	GGUACCU G CUUUAUC	1558	GAUUAAG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AAGGUACC	10220
2549	CUUUUCU G ACAUUCAU	1559	AUGAAUG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGGAAAG	10221
2560	AUUAUUU G CAGGAGGA	1560	UCCUCCU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AAUUGAAU	10222
2576	ACAUGUU G AUGAUGU	1561	ACAUAU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AACAAUGU	10223
2615	CAGUAAU G AAAACAGG	1562	CCUGUUU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AUUAACUG	10224
2641	UUAACUAG G CCUGCUAG	1563	CUAGCUG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AUAGUUAU	10225
2645	CUUGCCU G CUAGGUUU	1564	AAACUAG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGGCUAUG	10226
2677	AAUAUUU G CCCUAGA	1565	UCUAAGG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AAUAUUU	10227
2740	UUCAGAC G CGACAUUA	1566	UAUUGUG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GUCUGGAA	10228
2742	CCAGACG G ACAUUAUU	1567	AAUAUGU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GCGUCUGG	10229
2804	CACGUAG G CCUCAUUU	1568	AAUAGG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GCUACGUG	10230
2814	CUCAUUU G CGGGUCAC	1569	GUGACCG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AAAUGAG	10231
2875	CAAACUC G AAAAGGCA	1570	UGCCUUU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GAGGUUUG	10232
2928	UCUCCCC G AUCAUCAG	1571	CUGAUGU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GGGGAAGA	10233
2946	UGGACCU G CAUUCAAA	1572	UUUGAUG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGGUCCA	10234
2990	CUCAACC G CACAAGGA	1573	UCCUUGU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GGUUGAG	10235
3012	GGCCGAC G CCAACAAG	1574	CUUGUUG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GUCCGCC	10236
3090	GCCUCAC G CUCAGGGC	1575	GCCUGAG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG GUGAGGC	10237
3113	ACAACUG G CCAGCAGC	1576	GCUGUGG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG ACAGUUGU	10238
3132	CUCUCCU G CUCCACC	1577	GGUGGAG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGGAGGAG	10239
51	AGGGCCU G UACUUUCC	1578	GGAAAGU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGGGCCU	10240
106	AGAAUACU G UCUCUGCC	1579	GGCAGAG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGUAUUCU	10241
148	GGGACCU G UACCGAAC	1580	GUUCGGU GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGGUCCC	10242
198	CUGUCUGU G UACAGGC	1581	GCCUGUA GGAGAAACUCC CU UCAAGGACAUCGUCGCGG ACAGCAG	10243
219	UUUUUUU G UUGACAAA	1582	UUUGUCA GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGAATAA	10244
297	ACACCCU G UGUUUUG	1583	CCAAGAC GGAGAAACUCC CU UCAAGGACAUCGUCGCGG ACGGUGU	10245
299	ACCCGUGU G UCUUGGCC	1584	GGCCAAG GGAGAAACUCC CU UCAAGGACAUCGUCGCGG ACACGGU	10246
347	ACCAACU G UUGUCCUC	1585	GAGGACA GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AGGUUGU	10247
350	AACUGUU G UCCUCAA	1586	UUGGAGA GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AACAGUU	10248
362	UCCAUUU G UCCUGGU	1587	AACCAGA GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AAUUGGA	10249
381	CGUGGAU G UGUUGCG	1588	CGCAGAC GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AUCCAGG	10250
383	CUGGAUGU G UCUGCGG	1589	GCCGAGA GGAGAAACUCC CU UCAAGGACAUCGUCGCGG ACAUCCAG	10251
438	AUCUUUU G UUGGUUCU	1590	AGAACCA GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AAGAGAU	10252
465	CAAGUAU G UUGCCCGU	1591	ACGGGCA GGAGAAACUCC CU UCAAGGACAUCGUCGCGG AUACCUUG	10253

476	GCCCGUUU G UCCUCUAA	1592	UUAGAGGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAACGGGC	10254
555	ACCUCUAAU G UUUCUCCUC	1593	GAGGAAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUAGAGGU	10255
566	UCCUCUAAU G UUGUCUGUA	1594	UAGAGCAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUGAGGGA	10256
572	AUGUUGCU G UACAAAAAC	1595	UUUUUGUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGCAACAU	10257
602	CUGCACCUC G UAUUCCCCA	1596	UGGGAUUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGGUGCAG	10258
694	UGCCAUUU G UUCAGUGG	1597	CCACUGAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAUUGGCA	10259
724	CCCCCAGU G UCUGGCUU	1598	AAGCCAGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGUGGGGG	10260
750	UGGAUGAU G UGGUUUUG	1599	CAAAACCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUCAUCCA	10261
771	CCAAGUCU G UACACAU	1600	AUGUUGUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGACUUGG	10262
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818	UUUCUUUU G UCUUUGG	1602	CCCAAGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAAGAAA	10264
888	UGGGAUUAU G UAAUUGG	1603	CCCAUUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUAUCCCA	10265
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944	AUCAAUAU G UGUUUUAG	1605	CUAAAACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUUUUGAU	10267
946	CAAAAUUG G UUUUAGGA	1606	UCCUAAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACAUUUG	10268
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991	GAAGUAU G UCAACGAA	1608	UUCGUUGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUACUUUC	10270
1002	AACGAUU G UGGUCUU	1609	AAGACCCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAUUCGUU	10271
1039	CACGCAU G UGGAUAUU	1610	AAUAUCCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUUGCGUG	10272
1137	AACAGUAU G UGAACCUU	1611	AAGGUUCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUACUGUU	10273
1184	UGCCAAU G UUUGCUGA	1612	UCAGCAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACUUGGCA	10274
1251	GAACCUUU G UGUCUCCU	1613	AGGAGACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAGGUUC	10275
1253	ACCUUUGU G UCUCUUCU	1614	AGAGGAGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACAAGGU	10276
1294	AGCCGCUU G UUUUGCUC	1615	GAGCAAAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAGCGGU	10277
1344	ACAAUUCU G UCGUGCUC	1616	GAGCACGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGAAUUGU	10278
1390	GUAGGCU G UGUGGCCA	1617	UGGCAGCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGCCUAGC	10279
1425	CGUCCUUU G UUUAGGUC	1618	GACGUAAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAGGACG	10280
1508	CGCCUAAU G UACCGACC	1619	GGUCGGUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAUAGGCG	10281
1557	CCCCGUCU G UGCCUUUCU	1620	AGAAGGCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGACGGGG	10282
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1684	UCAGCAAU G UCAACGAC	1622	GUCGUUGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUUGCUGA	10284
1719	CAAAGACU G UGUUUUA	1623	UAAACACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGUCUUUG	10285
1721	AAGACUGU G UGUUUAAU	1624	AUUAAACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACAGUCUU	10286
1723	GACUGUGU G UUUUAUGA	1625	UCAUUAAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACACAGUC	10287
1772	AGGUUUUU G UACUAGGA	1626	UCCUAGUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAGACCU	10288
1785	AGGAGGCU G UAGGCAUA	1627	UAUGCCUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGCTUCCU	10289
1801	AAAUUGGU G UGUUACAC	1628	GGUGAACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACCAAUUU	10290

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1850	CAUCUCAU G UUCAUGUC	1630	GACAUGAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AUGAGAUG	10292
1856	AUGUUCU G UCCUACUG	1631	CAGUAGGA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AUGAACAU	10293
1864	GUCCUACU G UUCAAGCC	1632	GGCUUGAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGUAGGAC	10294
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2013	UCUGUCU G UAUCCGGG	1635	CCCCGAUA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGAGCAGA	10297
2045	GGAACAU G UUCACCUC	1636	GAGGUGAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AAUGUCC	10298
2082	GCUAUUCU G UGUUGGGG	1637	CCCCAACA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGAAUAGC	10299
2084	UAUUCUGU G UUGGGGUG	1638	CACCCCAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG ACAGAAUA	10300
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2222	CAUUUCCU G UCUUACUU	1641	AAGUAAGA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGGAAAUG	10303
2245	GAGAAACU G UUCUUGAA	1642	UUCAAGAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGUUUUCUC	10304
2262	UAUUUGGU G UCUUUUGG	1643	CCAAAAGA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG ACCAAAUA	10305
2274	UUUGGAGU G UGGAUUCG	1644	CGAAUCCA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG ACUCCAAA	10306
2344	AAACUACU G UUGUUAGA	1645	UCUAAACA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGUAGUUU	10307
2347	CUACUGUU G UUAACAGA	1646	UCGUCUAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AACAGUAG	10308
2450	AUCUCAU G UUAUAUUA	1647	AAUACUAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AUUGAGAU	10309
2573	AGGACAUU G UUGAUAGA	1648	UCUAUCAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AAUGUCCU	10310
2583	UGAUAGAU G UAAGCAAU	1649	AUUGCUUA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AUCUAUCA	10311
2594	AGCAUUU G UGGGGCCC	1650	GGGCCCCA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AAUUGCUU	10312
2663	AUCCCAU G UUAUUAUA	1651	UUUAGUAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AUUGGGAU	10313
2717	CAGAGUUAU G UAGUUUAU	1652	AUUAACUA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AUACUCUG	10314
2901	AUCUUUCU G UCCCCAAU	1653	AUUGGGGA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGAAAGAU	10315
3071	GGGGGACU G UUGGGGUG	1654	CACCCCAA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGUCCCCC	10316
3111	UCACAAU G UGCCAGCA	1655	UGCUGGCA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AGUUGUGA	10317
40	AUCCCAGA G UCAGGGCC	1656	GGCCCUGA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UCUGGGAU	10318
46	GAGUCAGG G CCCUGUAC	1657	GUACAGGG GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCUGACUC	10319
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68	UGCUGGUG G CUCCAGUU	1659	AACUGGAG GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CACCAGCA	10321
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89	AACAGUGA G CCCUGCUC	1662	GAGCAGGG GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UCACUGUU	10324
120	GCCCAUUC G UCAAUUU	1663	AAGAUUGA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG GAUAUGGC	10325
196	CCCUGCUC G UGUUACAG	1664	CUGUAACA GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG GAGCAGGG	10326
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210	CAGCGGG G UUUUUUU	1666	AAGAAAA GGAGAAACUCC CU UCAAGGACAUUCGCGGG CCCGCCUG	10328
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258	CUAGACUC G UGGUGGAC	1668	GUCCACCA GGAGAAACUCC CU UCAAGGACAUUCGCGGG GAGUCUAG	10330
261	GACUGUG G UGGACUUC	1669	GAAGUCCA GGAGAAACUCC CU UCAAGGACAUUCGCGGG CACGAGUC	10331
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332	AAUCUCCA G UCACUCAC	1673	GUGAGUGA GGAGAAACUCC CU UCAAGGACAUUCGCGGG UGGAGAUU	10335
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729	ACUGUCUG G CUUUCAGU	1693	ACUGAAAG GGAGAAACUCC CU UCAAGGACAUUCGCGGG CAGACAGU	10355
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785	CAUCUUGA G UCCCUUUA	1698	UAAAGGA GGAGAAACUCC CU UCAAGGACAUUCGCGGG UCAAGAUG	10360
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898	AAUUGGA G UUGGGGCA	1700	UGCCCAA GGAGAAACUCC CU UCAAGGACAUUCGCGGG UCCCAAUU	10362
904	GAGUUGG G CACAUUGC	1701	GCAUUGG GGAGAAACUCC CU UCAAGGACAUUCGCGGG CCAACUC	10363
971	GUAAACAG G CCUAUUGA	1702	UCAUAGG GGAGAAACUCC CU UCAAGGACAUUCGCGGG CUGUUUAC	10364

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1016	CUUUUGG G UUUUGCGC	1705	GCGGCAAA GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCCAAAG	10367
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1225	GGCCUAG G CCAUCAGC	1719	GCUGAUGG GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUAUGGCC	10381
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1306	UGCUCGCA G CAGGUUCG	1723	CAGACCUG GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UGCGAGCA	10385
1310	GCGAGCAG G UCUGGGGC	1724	GCCCCAGA GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUGCUGCG	10386
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1347	AUUCUGUC G UGCUCUCC	1726	GGAGAGCA GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG GACAGAAU	10388
1379	UUUCCUAG G CUGCUAGG	1727	CCUAGCAG GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAUGGAAA	10389
1387	GCUGCUAG G CUGUGCUG	1728	CAGCACAG GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUAGCAGC	10390
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1517	UACCGACC G UCCACGGG	1735	CCCUGGGA GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG GGUCGGUA	10397
1526	UCCACGGG G CGCACCUU	1736	GAGGUGCG GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCCUGGGA	10398
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1766	GGUUAAG G UCUUUGUA	1748	UACAAAGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUUAACC	10410
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1789	GGCUGUAG G CAUAAAU	1750	AAUUUUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUACAGCC	10412
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1870	CUGUUCAA G CCUCCAAG	1753	CUUGGAGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUGAACAG	10415
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2031	GCCUAGA G UCUCGGGA	1762	UCCGGAGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCUAAGGC	10424
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2074	UCAGGCAA G CUAUUCUG	1765	CAGAAUAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUGCCUGA	10427
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2094	UGGGUGGA G UGAUGAA	1767	UUAUCUAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCACCCCA	10429
2107	UGAAUCUA G CCACUUG	1768	CCAGGUGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAGAUCUA	10430
2116	CCACUUGG G UGGGAAGU	1769	ACUCCCCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAGGUGG	10431
2123	GGUGGGAA G UAAUUUGG	1770	CCAAUUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUCCACCC	10432
2140	AAGAUGCA G CAUCCAGG	1771	CCUGGAGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGGAUCUU	10433
2155	GGGAUUA G UAGUCAGC	1772	GCUGACUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAAUCCCC	10434
2158	AAUAGUA G UCAGCUAU	1773	AUAGCUGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UACUAAUU	10435
2162	AGUAGUA G CUAUGUA	1774	UGACAUAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGACUACU	10436
2173	AUGUCAAC G UUAUAUUG	1775	CAUAUUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GUUGACAU	10437
2183	UAAUAUGG G CCUAAAA	1776	UUUUUAGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAUAUUA	10438

2208	CUAUUGUG G UUUACAU	1777	AUGUAAA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CACAUAAG	10439
2235	ACUUUUG G CGAGAAAC	1778	GUUUUCG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CCAAAAGU	10440
2260	AAUAUUG G UGUUUUU	1779	AAAAGAC GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CAAUAUUT	10441
2272	CUUUUGGA G UUGUGAU	1780	AAUCCAC GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UCCAAAAG	10442
2360	ACGAAGAG G CAGGUCCC	1781	GGGACUG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUCUUUGU	10443
2364	AGAGGAG G UCCCUAG	1782	CUAGGGA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUGCCUCU	10444
2403	AGACGAAG G UCUCAAUC	1783	GAUUGAG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUUGGUCU	10445
2417	AUCGCCG G UGCAGAA	1784	UUCUGCA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG GCGGCGAU	10446
2454	CAAUUUU G UAUUCCU	1785	AAGGAUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UAACAUUG	10447
2474	CACAUAG G UGGGAAAC	1786	GUUUCCA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUUAUGUG	10448
2491	UUUACGG G CUUUUUU	1787	GAUUAAG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CCGUAAA	10449
2507	CUUCVAC G UACCUUG	1788	GCAAGUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CGUAGAAG	10450
2530	CCUAAUG G CAAACUCC	1789	GGGUUUG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CAUUUAGG	10451
2587	AGAUUAA G CAAUUUG	1790	ACAAUUG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UUAUAUCU	10452
2599	UUUGUGG G CCCUUAC	1791	GUAGGGG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CCAACAAA	10453
2609	CCUUACA G UAAUUGA	1792	UUAUUUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UGUAAAGG	10454
2650	CCUGUAG G UUUUAUCC	1793	GGUAAAA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUAGCAGG	10455
2701	AUCAAAC G UAUUAUCC	1794	GGUAAUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG GGUUUUGU	10456
2713	UAUCAGA G UAUUGAU	1795	ACUACUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UCUGGAUA	10457
2720	AGUAUGA G UUAUAU	1796	AUGAUUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UACUAUCU	10458
2768	UUUGAAG G CGGGGAUC	1797	GAUCCCG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUUCCAAA	10459
2791	AAAGAGA G UCCACAG	1798	CGUGUGA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UCUCUUUU	10460
2799	GUCCACAC G UAGGCCU	1799	AGGCGUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG GUGUGGAC	10461
2802	CACACUA G CGCCUCA	1800	AUGAGGG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UACGUGUG	10462
2818	UUUUGCG G UCACCAU	1801	UAUGGUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CCGCAAAA	10463
2848	GAUCUAC G CAUGGGAG	1802	CUCCCAU GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UGUAGAUC	10464
2857	CAUGGGAG G UUGGUCU	1803	AAGACCA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUCCCAUG	10465
2861	GGAGGUG G UCUUCCAA	1804	UUGGAUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CAACCUCC	10466
2881	UCGAAAAG G CAUGGGGA	1805	UCCCAUG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUUUUGCA	10467
2936	GAUCAUA G UUGGACCC	1806	GGGUCAA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UGAUGAUC	10468
2955	CAUUCAAA G CCAACUCA	1807	UGAGUUG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UUUAAAUG	10469
2964	CCAACUA G UAAAUCCA	1808	UGAUUUA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UGAGUUGG	10470
3005	GACAAUG G CCGGACGC	1809	GCGUCGG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CAGUUGUC	10471
3021	CCAACAAG G UGGGAGUG	1810	CACUCCA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CUUGUUGG	10472
3027	AGGUGGGA G UGGGAGCA	1811	UGCUCCA GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UCCACCU	10473
3033	GAGUGGGA G CAUUCGGG	1812	CCGGAUG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG UCCACUC	10474
3041	GCAUUCG G CCAGGGUU	1813	AACCCUG GGAGGAAAUCC CU UCAAGGACAUUCGUCGGG CCGAAUGC	10475

3047	GGGCAGG G UUCACCCC	1814	GGGUGAA GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CCUGGCCC	10476
3077	CUGUUGG G UGGAGCCC	1815	GGGUCCA GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CCACACAG	10477
3082	GGGUGGA G CCUCACG	1816	CGUGAGG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UCCACCCC	10478
3097	CGUCAGG G CCUACUA	1817	UGAGUAGG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CCUGAGCG	10479
3117	CUGUGCCA G CAGCUCCU	1818	AGGAGCUG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGGCACAG	10480
3120	UGCCAGCA G CUCCUCCU	1819	AGGAGAG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGCUGGCA	10481
3146	ACCAUUG G CAGUCAGG	1820	CCUGACUG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CGAUUGGU	10482
3149	AUUGGCA G UCAGGAAG	1821	CUUCCUGA GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGCCGAUU	10483
3158	UCAGGAAG G CAGCCUAC	1822	GUAGGCUG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CUUCCUGA	10484
3161	GGAAGGCA G CCUACUCC	1823	GGAGUAGG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGCCUUC	10485
3204	AUCCUCAG G CCAUGCAG	1824	CUGCAUGG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CUGAGGAU	10486
31	CUCUCAA G AUCCGAGA	1999	UCUGGGAU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UUGAAGAG	10487
38	AGAUCCCA G AGUCAGGG	2000	CCUGACU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGGGAUCU	10488
44	CAGAGUCA G GGCCUUGU	2001	ACAGGCG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGACUCUG	10489
45	AGAGUCAG G GCCUGUA	2002	UACAGGC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CUGACUCU	10490
64	UUCUGCU G GUGGCUC	2003	GGAGCAC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG AGCAGGAA	10491
67	CUGCUGG G GCUCCAGU	2004	ACUGGAG GGAGGAAACUCC CU UCAAGGACAUUCUCCGG ACCAGCAG	10492
79	CCAGUUA G GAACAGUG	2005	CACUGUUC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGAACUGG	10493
80	CAGUUCAG G AACAGUGA	2006	UCACUGU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CUGAACUG	10494
99	CCUGCUCA G AAUACUGU	2007	ACAGUAU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGAGCAGG	10495
135	UUAUGGA G ACUGGGGA	2008	UCCGAGU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UUCGAUAA	10496
139	CGAAGACU G GGGACCCU	2009	AGGUCCC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG AGUCUUCG	10497
140	GAAGACUG G GGACCCUG	2010	CAGGUCC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CAGUCUUC	10498
141	AAGACUGG G GACCCUGU	2011	ACAGGUC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CCAGUCUU	10499
142	AGACUGG G ACCCUGUA	2012	UACAGGU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CCAGUCU	10500
159	CCGAACAU G GAGAACAU	2013	AUGUUCU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG AUGUUCGG	10501
160	CGAACAU G AGAACAU	2014	GAUGUUC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CAUGUUCG	10502
162	AACAUGGA G AACAUCCG	2015	GCGAUGU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UCCAUGUU	10503
175	UCGAUCA G GACUCCUA	2016	UAGGAGU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGAUGCGA	10504
176	CGCAUCAG G ACUCCUAG	2017	CUAGGAGU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CUGAUGCG	10505
184	GACUCCUA G GACCCUUG	2018	CAGGGUC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UAGGAGUC	10506
185	ACUCCUAG G ACCCCUGC	2019	GCAGGGU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CUAGGAGU	10507
204	GUGUACA G GCGGGGUU	2020	AACCCGC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGUAAACAC	10508
207	UACAGGC G GGGUUUUU	2021	AAAAACC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG GCCUGUAA	10509
208	UACAGGC G GGUUUUUC	2022	GAATAAC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CGCUGUA	10510
209	ACAGGCG G GUUUUUUC	2023	AGAAAC GGAGGAAACUCC CU UCAAGGACAUUCUCCGG CCGCCUGU	10511
246	AUACACA G AGUCUAGA	2024	UCUAGAU GGAGGAAACUCC CU UCAAGGACAUUCUCCGG UGUGUAU	10512

253	AGAGUCUA G ACUCGUGG	2025	CCACGAGU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UAGACUCU	10513
260	AGACUCGU G GUGGACUU	2026	AAGUCCAC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG ACAGUCU	10514
263	CUCGUGGU G GACUUCUC	2027	GAGAAAGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG ACCACGAG	10515
264	UCGUGGUG G ACUUCUCU	2028	AGAGAAGU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CACCACGA	10516
283	AUUUUCUA G GGGGRACA	2029	UGUUCGCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UAGAAAAU	10517
284	UUUUCUAG G GGGACAC	2030	GUGUUCGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUAGAAAA	10518
285	UUUCUAGG G GGAACACC	2031	GGUGUUCG GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCUAGAAA	10519
286	UUUCUAGG G GAACACCC	2032	GGGUGUUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCUAGAAA	10520
287	UCUAGGGG G AACACCCG	2033	CGGGUGUU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCCUAGA	10521
304	UGUGUCUU G GCCRAAAU	2034	AUUUUGGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AAGACACA	10522
367	UUUGUCCU G GUUAUGGC	2035	GCGAUAAC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AGGACAAA	10523
377	UUAUCGCU G GAUGUGUC	2036	GACACAUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AGCGAUAA	10524
378	UAUCGCGU G AUGUGUCU	2037	AGACACAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAGCGAUA	10525
389	GUGUCUGC G GCGUUUUA	2038	UAAAACGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG GCAGACAC	10526
441	UUCUUGUU G GUUCUUCU	2039	AGAAGAAC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AACAAAGAA	10527
450	GUUCUUCU G GACUAUCA	2040	UGAUAGUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AGAAGAAC	10528
451	UUCUUCUG G ACUAUCA	2041	UUGAUAGU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAGAAGAA	10529
460	ACUAUCA G GUUAUGUG	2042	CAACAUAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UUGAUAGU	10530
490	UAAUCCA G GAUCAUCA	2043	UGAUGAUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UGGAUUUA	10531
491	AUUUCCAG G AUCAUCA	2044	UUGAUGAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUGGAUUU	10532
511	CCAGCAC G GACCAUGC	2045	GCAUGGUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG GGUGUCUG	10533
512	CAGCACCG G ACCAUGCA	2046	UGCAUGGU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CGGUCUGG	10534
544	UGUCUCA G GAACUCUC	2047	AGAGGUUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UUGAGCAG	10535
545	UGUCUCA G GAACUCUC	2048	UAGAGGUU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUUGAGCA	10536
585	AAACCUAC G GACGGAAA	2049	UUUC'CGUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG GUAGGUUU	10537
586	AACCUACG G ACGGAAAC	2050	GUUUC'CGU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CGUAGGUU	10538
589	CUACGGAC G GAAACUGC	2051	GCAGUUUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG GUCCGUAG	10539
590	UACGGACG G AAACUGCA	2052	UGCAGUUU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CGUCCGUA	10540
623	AUCAUUG G GGUUUUG	2053	CGAAAGCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AAGAUGAU	10541
624	UCAUUGG G GGUUUUG	2054	GCGAAAGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAAGAUGA	10542
644	AUACCUAU G GAGUGGGG	2055	CCCACUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AUAGGUUU	10543
645	UACCUAUG G GAGUGGGC	2056	GCCCACUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAUAGGUA	10544
646	ACCUAUGG G AGUGGGCC	2057	GGCCACAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCAUAGGU	10545
650	UGGGAGU G GGCUCAG	2058	CUGAGGCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG ACUCCCAU	10546
651	UGGGAGU G GGCUCAG	2059	ACUGAGGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CACUCCCA	10547
671	UUUCUUCU G GCUCAGUU	2060	AACUGAGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AAGAGAAA	10548
701	UGUUCAGU G GUUCGUAG	2061	CUACGAAC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG ACUGAACA	10549

709	GGUUCGUA G GGUUUUCC	2062	GGAAAGCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UACGAACC	10550
710	GUUCGUAG G GCUUUCCC	2063	GGGAAAGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUACGAAC	10551
728	CACUGUCU G GCUUUCAG	2064	CUGAAAGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AGACAGUG	10552
743	AGUUUAU G GAUGAUGU	2065	ACAUCUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AUUAUAACU	10553
744	GUUAUAG G AUGAUGUG	2066	CACAUAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAUAUAAC	10554
752	GAUGAUGU G GUUUUGGG	2067	CCCAAAAC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG ACAUCAUC	10555
758	GUGGUUUU G GGGCCCAA	2068	UUGGCCCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AAAACCAC	10556
759	UGGUUUUG G GGGCCAAAG	2069	CUUGGCCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAAAACCA	10557
760	GGUUUUUG G GGCCAAAGU	2070	ACUUGGCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCAAAACC	10558
761	GUUUUGGG G GCCAAGUC	2071	GACUUGGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCCAAAAC	10559
824	UUGUCUUU G GGUUAUACA	2072	UGUAUACC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AAAGACAA	10560
825	UGUCUUUG G GUUAUACAU	2073	AUGUAUAC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAAAGACA	10561
856	AACAAAA G AUGGGGAU	2074	AUCCCAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UUUUUGUU	10562
859	AAAAAGAU G GGAUAUU	2075	AAUAUCCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AUCUUUUU	10563
860	AAAAGAU G GGAUAUUC	2076	GAUAUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAUCUUUU	10564
861	AAAGAUUG G GAUAUUC	2077	GGAAUAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCAUCUUU	10565
862	AAGAUUGG G AUAUUCCC	2078	GGGAUAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCAUCUUU	10566
881	AACUUAU G GGAUAUGU	2079	ACAUAUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AUGAAGUU	10567
882	ACUUAUG G GAUAUGUA	2080	UACAUAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAUGAAGU	10568
883	CUUCAUGG G AUAUGUAA	2081	UUACAUAU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCAUGAAG	10569
894	AUGUAUU G GGAGUUGG	2082	CCAACUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AAUAUACU	10570
895	UGUAUUUG G GAGUUGGG	2083	CCCAACUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAAUUAUA	10571
896	GUAAUUUG G AGUUGGGG	2084	CCCCAACU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCAAUUAC	10572
901	UGGGAGUU G GGGCACAU	2085	AUGUGCCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AACUCCCA	10573
902	GGGAGUUG G GGCACAUU	2086	AAUGUGCC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAACUCCC	10574
903	GGAGUUGG G GCACAUUG	2087	CAAUGUGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CCAACUCC	10575
917	UUGCCACA G GAACAUAU	2088	AUAUGUUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UGUGGCAA	10576
918	UGCCACAG G AACAUUUU	2089	AAUAUGUU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUGUGGCA	10577
952	GUGUUUUA G GAAACUUC	2090	GAAGUUUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UAAAAAC	10578
953	UGUUUUAG G AAACUUCU	2091	GGAGUUUU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CUAAAAAA	10579
970	UGUAAACA G GCUUAUUG	2092	CAAUAGGC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG UGUUUACA	10580
982	UAUUAUU G GAAAGUAU	2093	AUAUUUUC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AAUCAAUU	10581
983	AUUAUUG G AAAGUAUG	2094	CAUAUUUU GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAAUCAAU	10582
1004	CGAAUUGU G GGUUUUUU	2095	AAAAGACC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG ACAAUUCG	10583
1005	GAAUUGUG G GUCUUUUU	2096	CAAAAGAC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CACAUAUC	10584
1013	GGUCUUUU G GGGUUUUG	2097	GCAAAACC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG AAAAGACC	10585
1014	GUCUUUUU G GGUUUUGC	2098	GGCAAAAC GGAGGAAACUCC CU UCAAGGACAUUCGUCCGGG CAAAAGAC	10586

1015	UCUUUGG G GUUUGCG	2099	CGCAAC GGAGAAAUCC CU UCAAGGACAUUGUCCGG CCAAGA	10587
1041	CGCAUUG G GAUAUUCU	2100	AGAAUUC GGAGAAAUCC CU UCAAGGACAUUGUCCGG ACAUUGC	10588
1042	GCAUUGG G AUAUUCU	2101	CAGAAUUC GGAGAAAUCC CU UCAAGGACAUUGUCCGG CACAUGC	10589
1088	GCAAAACA G GCUUUUAC	2102	GUAAAGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG UGUUUUGC	10590
1115	ACUUAACA G GCCUUUCU	2103	AGAAAGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG UUGUAAGU	10591
1159	CGUUGUC G GCAACGGC	2104	GCCUUGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GAGCAACG	10592
1165	UCGGCAAC G GCCUGGUC	2105	GACCAGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GUUGCCGA	10593
1170	AACGGCTU G GUCUAUGC	2106	GCAUAGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG AGGCCGUU	10594
1206	CCCCACU G GUUGGGG	2107	GCCCCAC GGAGAAAUCC CU UCAAGGACAUUGUCCGG AGUGGGG	10595
1210	CACUGGU G GGGCUUG	2108	CCAAGCC GGAGAAAUCC CU UCAAGGACAUUGUCCGG AACCAUG	10596
1211	ACUGGUU G GGCUGGC	2109	GCCAAGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG CAACCAU	10597
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1217	UGGGGUU G GCCAUAGG	2111	CCUAUGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG AAGCCCCA	10599
1224	UGGCCAU G GCCAUAG	2112	CUGAUGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG UAUGGCCA	10600
1242	GCAUGGU G GAACUUU	2113	AAAGGUU GGAGAAAUCC CU UCAAGGACAUUGUCCGG ACGAUGC	10601
1243	CAUGGUG G AACUUUG	2114	CAAGGUU GGAGAAAUCC CU UCAAGGACAUUGUCCGG CACGAUG	10602
1277	CAUACGC G GAACUCCU	2115	AGAGUUC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GCGUAUG	10603
1278	AUACGGG G AACUCCUA	2116	UAGAGUU GGAGAAAUCC CU UCAAGGACAUUGUCCGG GCGGUUU	10604
1309	UCGACGA G GUCUGGG	2117	CCCCAGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG UGUGCGA	10605
1314	GCAGGUU G GGGCAAAA	2118	UUUUGCC GGAGAAAUCC CU UCAAGGACAUUGUCCGG AGACUUG	10606
1315	CAGGUUG G GGCAAAAC	2119	GUUUGCC GGAGAAAUCC CU UCAAGGACAUUGUCCGG CAGACUUG	10607
1316	AGGUUGG G GCAAAACU	2120	AGUUUGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG CCAGACCU	10608
1329	AACUACU G GGACUGAC	2121	GUCAGUC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GAUGAGUU	10609
1330	ACUACUG G GACUGACA	2122	UGUCAGU GGAGAAAUCC CU UCAAGGACAUUGUCCGG CGAUGAG	10610
1331	CUCAUGG G ACUGACAA	2123	UUGUCAGU GGAGAAAUCC CU UCAAGGACAUUGUCCGG AUGGAAU	10611
1378	AUUUCCAU G GCUUGUAG	2124	CUAGCAGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG CCGAUGAG	10612
1386	GGUGGUA G GCUUGU	2125	AGCACAGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG UAGCAGC	10613
1402	UGCCAAU G GAUCCUAC	2126	GUAGGAC GGAGAAAUCC CU UCAAGGACAUUGUCCGG AGUUGCA	10614
1403	GCCAAUG G AUCCUACG	2127	CGUAGGAU GGAGAAAUCC CU UCAAGGACAUUGUCCGG CAGUUGC	10615
1413	UCCUACG G GGACGUCC	2128	GGACGUCC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GCGUAGGA	10616
1414	CCUACCG G GACGUCCU	2129	AGGACGUC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GCGUAGG	10617
1415	CUACGGG G ACUGUCCU	2130	AAGGACGU GGAGAAAUCC CU UCAAGGACAUUGUCCGG CCGCGUAG	10618
1439	GUCCGUC G GCGUGAA	2131	UUCAGCGC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GACGGGAC	10619
1454	AAUCCGC G GACGACCC	2132	GGGUCGUC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GCGGGAU	10620
1455	AUCCGCG G ACGACCCC	2133	GGGUGUCU GGAGAAAUCC CU UCAAGGACAUUGUCCGG GCGGGAU	10621
1468	CCCUCCC G GGGCCGCU	2134	AGCGGCC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GGGAGGG	10622
1469	CCUCCCG G GCGCGCU	2135	AAGCGCC GGAGAAAUCC CU UCAAGGACAUUGUCCGG GGGAGGG	10623

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1480	CGCUUGG G GCUUACC	2139	GUAGAGC GGAGAAACUCC CU UCAAGGACAUUCUCCGG CCAAGCGG	10627
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1525	GUCCACG G GGCACCU	2142	AGGUGCG GGAGAAACUCC CU UCAAGGACAUUCUCCGG CCGUGGAC	10630
1544	CUUACGC G GACUCCC	2143	GGGAGUC GGAGAAACUCC CU UCAAGGACAUUCUCCGG CGGUAAG	10631
1545	UUUACGC G ACUCCCC	2144	CGGGAGU GGAGAAACUCC CU UCAAGGACAUUCUCCGG GCGUAAA	10632
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1613	GUCGCAU G AGACCAC	2148	GGUGUCU GGAGAAACUCC CU UCAAGGACAUUCUCCGG CAUCGAC	10636
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1635	CGCCACA G GAACCGU	2150	GCAGGUC GGAGAAACUCC CU UCAAGGACAUUCUCCGG UGUGGGC	10638
1636	GCCACAG G AACUGCC	2151	GGCAGGU GGAGAAACUCC CU UCAAGGACAUUCUCCGG CUGUGGC	10639
1648	CUGCCAA G GUCUUGA	2152	UGCAAGC GGAGAAACUCC CU UCAAGGACAUUCUCCGG UUGGCGAG	10640
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1663	CAUAAG G ACUCUUG	2155	CCAAGU GGAGAAACUCC CU UCAAGGACAUUCUCCGG CUCUUAUG	10643
1670	GGACUCU G GACUUUA	2156	UGAAAGC GGAGAAACUCC CU UCAAGGACAUUCUCCGG AAGAGUCC	10644
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1715	ACUUCAA G ACUGUGU	2159	CACACAGU GGAGAAACUCC CU UCAAGGACAUUCUCCGG UUUGAAGU	10647
1734	UAUAGAGU G GGAGGAGU	2160	ACUCCUC GGAGAAACUCC CU UCAAGGACAUUCUCCGG ACUCAUUA	10648
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1751	UGGGGAG G AGGUUAGG	2171	CUAACUC GGAGAAACUCC CU UCAAGGACAUUCUCCGG CUCCCCA	10659
1753	GGGAGGA G GUUAGGU	2172	AACCUAAC GGAGAAACUCC CU UCAAGGACAUUCUCCGG UCCUCCC	10660

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1778	UGUACUA G GAGGUGU	2175	ACAGCCUC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UAGUACAA	10663
1779	UGUACUAG G AGGUGUA	2176	UACAGCCU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CUAGUACA	10664
1781	UACUAGGA G GCUGUAGG	2177	CUACAGC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UCUUAGUA	10665
1788	AGGUGUA G GCAUAAU	2178	AUUUAUGC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UACAGCCU	10666
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1889	GUGCCUUG G GUGGCUUU	2181	AAAGCCAC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CAAGGCAC	10669
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1898	GUGGCUUU G GGGCAUGG	2183	CCAUGCCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AAAGCCAC	10671
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1905	UGGGGCAU G GACAUUGA	2186	UCAAUGUC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AUGCCCCA	10674
1906	GGGGCAUG G ACAUUGAC	2187	GUCAUUGU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CAUGCCCC	10675
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1941	GUUCUGU G GAGUUAU	2191	AGUAAACU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG ACAGAAAG	10679
1942	CUUCUGUG G AGUUAACU	2192	GAGUAAU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CACAGAAAG	10680
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2019	CUGUAUCG G GGGGCCU	2195	AAGGCCCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CGAUACAG	10683
2020	UGUAUCGG G GGGCCUUA	2196	UAAGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCGAUACA	10684
2021	GUUCGGG G GGCUUUAG	2197	CUAAGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCGAUAC	10685
2022	UAUCGGG G GCCUAGA	2198	UCUAAGC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCCCAGUA	10686
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2182	UUAAUUG G GCCUAAA	2219	AUUAUUG GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CAUAUUA	10707
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2269	UGUCUUU G GAGUGUGG	2226	UGCGAAU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG ACACUCC	10714
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2300	UGCAUUA G ACCACCAA	2230	CUCUUCG GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG UUCGUCUA	10718
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2335	CACUCCG G AAGAAAGU	2232	GGACCCG GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG UGCGAGC	10720
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2887	AGGCAUG G GACAAAU	2299	GAUUUGUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CCAUGCCU	10787
2888	GGCAUGG G GACAAAU	2300	AGAUUUGU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CCAUGCC	10788
2915	AUCCCCU G GGAUUCUU	2301	AAGAAUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG AGGGGAU	10789
2916	AUCCCCU G GAUUCUUC	2302	GAAGAAUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CAGGGGAU	10790
2917	UCCCCUG G AUUCUUC	2303	GGAAGAAU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CCAAGGGGA	10791
2939	CAUCAGUU G GACCCUGC	2304	GCAGGUAU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG AACUGAUG	10792
2940	AUCAGUUG G ACCCUGCA	2305	UGCAGGUU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CAACUGAU	10793
2973	UAAAUCCA G AUUGGGAC	2306	GUCCCAAU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG UGGAUUAU	10794
2977	UCCAGAUU G GGACCUCA	2307	UGAGGUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG AAUCUGGA	10795
2978	CCAGAUUG G GACCUCAA	2308	UUGAGGUU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CAAUCUGG	10796
2979	CAGAUUGG G ACCUCAAC	2309	GUUGAGGU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CCAUCUG	10797
2996	CCGACAA G GACAAUUG	2310	CAGUUGU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG UUGUGCGG	10798
2997	CGCACAA G ACAACUGG	2311	CCAGUUGU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CUUGUGCG	10799
3004	GGACAACU G GCGGGACG	2312	CGUCCGCG GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG AGUUGUCC	10800
3008	AACUGGCC G GACGCCAA	2313	UUGCGUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG GGCCAGUU	10801
3009	ACUGGCCG G AGGCCAAC	2314	GUUGCGGU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CGGCCAGU	10802
3020	GCCACAA G GUGGGAGU	2315	ACUCCAC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG UUGUUGGC	10803
3023	AACAAGU G GGAGUGG	2316	CCGACUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG ACCUUGUU	10804
3024	ACAAGGUG G GAGUGGGA	2317	UCCACUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CACCUUGU	10805
3025	CAAGGUGG G AGUGGGAG	2318	CUCCACU GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CCACCUUG	10806
3029	GUGGGAGU G GGAGCAUU	2319	AUUGUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG ACUCCAC	10807
3030	UGGGAGUG G GAGCAUUC	2320	GAAUGUCC GGAGGAAACUCC CU UCAAGGACAUUCGUCGGG CACUCCCA	10808

3031	GGGAGUGG G AGCAUUCG	2321	CGAAUGCU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCACUCCC	10809
3039	GAGCAUUC G GGCCAGGG	2322	CCCUGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG GAAUGCUC	10810
3040	AGCAUUCG G GCCAGGGU	2323	ACCCUGGC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CGAAUGCU	10811
3045	UCGGGCCA G GGUUCACC	2324	GGUGAAC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UGSCCCGA	10812
3046	CGGGCCAG G GUUCACCC	2325	GGUGAAC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CUGGCCCG	10813
3063	CUCCCCAU G GGGGACUG	2326	CAGUCCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AUGGGGAG	10814
3064	UCCCCAUG G GGGACUGU	2327	ACAGUCCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CAUGGGGA	10815
3065	CCCCAUGG G GGACUGUU	2328	AACAGUCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCAUGGGG	10816
3066	CCCAUGGG G GACUGUUG	2329	CAACAGUC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCAUUGGG	10817
3067	CCAUGGGG G ACUGUUGG	2330	CCAACAGU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCCC AUGG	10818
3074	GGACUGUU G GGGUGGAG	2331	CUCCACCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG AACAGUCC	10819
3075	GACUGUUG G GGUGGAGC	2332	GCUCACC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CAACAGUC	10820
3076	ACUGUUGG G GUGGAGCC	2333	GGUCCAC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCAACAGU	10821
3079	GUUGGGGU G GAGCCUUC	2334	GAGGCUC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG ACCCCAAC	10822
3080	UUGGGGUG G AGCCCUCA	2335	UGAGGCU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CACCCCAA	10823
3095	CACGCUCA G GGCCUACU	2336	AGUAGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UGAGCGUG	10824
3096	ACGCUACG G GCCUACUC	2337	GAGUAGGC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CUGAGCGU	10825
3145	CACCAUUC G GCAGUCAG	2338	CUGACUGC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG GAUUGGUG	10826
3153	GGCAGUCA G GAAAGGCAG	2339	CUGCCUUC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UGACUGCC	10827
3154	GCAGUCAG G AAGGCAGC	2340	GCUGCCUU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CUGACUGC	10828
3157	GUACAGGA G GCAGCCUA	2341	UAGGCUUC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UCCUGAC	10829
3187	ACCUCUAA G GGACACUC	2342	GAGUGUCC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UAGAGGU	10830
3188	CCUCUAAG G GACACUCA	2343	UGAGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CUUAGAGG	10831
3189	CUCUAAGG G ACACUCAU	2344	AUGAGUGU GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG CCUAGAG	10832
3203	CAUCCUCA G GCCAUGCA	2345	UGCAUGGC GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG UGAGGAUG	10833

Input Sequence = AF100308. Cut Site = YG/M or UG/U.

Stem Length = 8. Core Sequence = GGAGGAAACUCC CU UCAAGGACAUCGUCGCGG
 AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

Table XI: Human HBV Enzymatic Nucleic Acid and Target Sequence

Pos	SUBSTRATE	Seq ID	RPI#	Ribozyme Alias	ENZYMATIC NUCLEIC ACID	Seq ID
313	CCAAAU U CGCAGUC	2346	18157	HBV-313 Rz-7 RNA	GACUGCG CUGAUGAGCCGUUAGGCCGAA AUUUUGG B	10834
327	CCCAAU C UCCAGUC	2347	18158	HBV-327 Rz-7 RNA	GACUGGA CUGAUGAGCCGUUAGGCCGAA AUUUUGG B	10835
334	CUCCAGU C ACUCACC	2348	18159	HBV-334 Rz-7 RNA	GGUGAGU CUGAUGAGCCGUUAGGCCGAA ACUGGAG B	10836
408	UCUUCU C UGCAUCC	2349	18160	HBV-408 Rz-7 RNA	GGAGUCA CUGAUGAGCCGUUAGGCCGAA AGGAAGA B	10837
557	UCUAUGU U UCCCUCA	2350	18161	HBV-557 Rz-7 RNA	UGAGGGA CUGAUGAGCCGUUAGGCCGAA ACAUAGA B	10838
1255	UUUGUGU C UCCUCUG	2351	18162	HBV-1255 Rz-7 RNA	CAGAGGA CUGAUGAGCCGUUAGGCCGAA ACACAAA B	10839
1538	CCUCUCU U UACGCCG	2352	18163	HBV-1538 Rz-7 RNA	CCCGGUA CUGAUGAGCCGUUAGGCCGAA AGAGAGG B	10840
1756	AGGAGGU U AGGUUAA	2353	18164	HBV-1756 Rz-7 RNA	UUAAACU CUGAUGAGCCGUUAGGCCGAA ACCUCCU B	10841
1861	AUGUCCU A CUGUUCA	2354	18165	HBV-1861 Rz-7 RNA	UGAACAG CUGAUGAGCCGUUAGGCCGAA AGGACAU B	10842
2504	UUCUUCU A CGGUACC	2355	18166	HBV-2504 Rz-7 RNA	GGUACCG CUGAUGAGCCGUUAGGCCGAA AGAAGAA B	10843
10	CUCCACC A CUUCCCA	2356	18197	HBV-10 CHZ-7 RNA	UGGAAAG CUGAUGAGCCGUUAGGCCGAA GGUGGAG B	10844
335	UCACGUC A CUCACCA	2357	18198	HBV-335 CHZ-7 RNA	UGGUGAG CUGAUGAGCCGUUAGGCCGAA GACUGGA B	10845
1258	GUGUCUC C UCUGCCG	2358	18199	HBV-1258 CHZ-7 RNA	CGGCAGA CUGAUGAGCCGUUAGGCCGAA GAGACAC B	10846
2307	GACCACC A AAUCCCC	2359	18200	HBV-2307 CHZ-7 RNA	GGGCAU CUGAUGAGCCGUUAGGCCGAA GGUGGUC B	10847
347	UCACCACCU G UUGUC	2360	18216	HBV-347 GCL.Rz-5/10 RNA	GACAA UGAUGGCAUGCACUAUGCCG AGGUUGUGA B	10848
350	CCAACCUUU G UCCUC	2361	18217	HBV-350 GCL.Rz-5/10 RNA	GAGGA UGAUGGCAUGCACUAUGCCG AACAGGUUG B	10849
1508	UCCGCCUAU G UACCG	2362	18218	HBV-1508 GCL.Rz-5/10 RNA	CGGUA UGAUGGCAUGCACUAUGCCG AAUAGGCCG B	10850
234	AAUCCU C ACAUA	2363	18334	HBV-234 Rz-6 allyl stabl	u ₈ a ₈ u ₈ gu CUGAUGagggccguuagggccGaa Aggaau B	10851
252	GAGUCU A GACUCG	2364	18335	HBV-252 Rz-6 allyl stabl	c ₈ g ₈ a ₈ g ₈ uc CUGAUGagggccguuagggccGaa Agacuc B	10852
268	UGGACU U CUCUCA	2365	18337	HBV-268 Rz-6 allyl stabl	u ₈ g ₈ a ₈ g ₈ g CUGAUGagggccguuagggccGaa Agucca B	10853
280	AAUUU C UAGGGG	2366	18345	HBV-280 Rz-6 allyl stabl	c ₈ c ₈ c ₈ ua CUGAUGagggccguuagggccGaa Aaaaau B	10854
313	CAAAU U CGCAGU	2367	18346	HBV-313 Rz-6 allyl stabl	a ₈ c ₈ u ₈ g ₈ cg CUGAUGagggccguuagggccGaa Auuuug B	10855
395	GGCGUU U UAUCAU	2368	18350	HBV-395 Rz-6 allyl stabl	a ₈ u ₈ g ₈ a ₈ ua CUGAUGagggccguuagggccGaa Aacgcc B	10856
402	UAUCAU C UUCCUC	2369	18351	HBV-402 Rz-6 allyl stabl	g ₈ a ₈ g ₈ g ₈ aa CUGAUGagggccguuagggccGaa Augaau B	10857
607	UGUAUU C CCAUCC	2370	18355	HBV-607 Rz-6 allyl stabl	g ₈ g ₈ a ₈ u ₈ g ₈ g CUGAUGagggccguuagggccGaa Auauca B	10858
697	UUUGUU C AGUGGU	2371	18362	HBV-697 Rz-6 allyl stabl	a ₈ c ₈ c ₈ a ₈ cu CUGAUGagggccguuagggccGaa Aaaaa B	10859
1539	UCUCUU U ACGCGG	2372	18366	HBV-1539 Rz-6 allyl stabl	c ₈ s ₈ g ₈ c ₈ g ₈ u CUGAUGagggccguuagggccGaa Aagaga B	10860
1599	UCACCU C UGCACG	2373	18367	HBV-1599 Rz-6 allyl stabl	c ₈ g ₈ u ₈ g ₈ ca CUGAUGagggccguuagggccGaa Agguga B	10861
1607	GCACGU C GCAUGG	2374	18368	HBV-1607 Rz-6 allyl stabl	c ₈ c ₈ a ₈ u ₈ g ₈ c CUGAUGagggccguuagggccGaa Acgucg B	10862
1833	UCACCU C UGCCUA	2375	18371	HBV-1833 Rz-6 allyl stabl	u ₈ a ₈ g ₈ g ₈ ca CUGAUGagggccguuagggccGaa Agguga B	10863

2383	AGAAGU C CCUGC	2376	18374	HBV-2383 Rz-6 allyl stabl	g ₅ c ₅ g ₅ a ₅ g ₅ g cUGAuGagggccgguuagggccGaa	10864
2429	GAAGAU C UCAAU	2377	18376	HBV-2429 Rz-6 allyl stabl	g ₅ a ₅ u ₅ u ₅ g ₅ a cUGAuGagggccgguuagggccGaa	10865
2831	UAUUCU U GGAAC	2378	18379	HBV-2831 Rz-6 allyl stabl	g ₅ u ₅ u ₅ c ₅ g ₅ cc cUGAuGagggccgguuagggccGaa	10866
430	UGCCUC A UCUUCU	2379	18391	HBV-430 CHz-6 allyl stabl	a ₅ g ₅ a ₅ g ₅ a cUGAuGagggccgguuagggccGaa	10867
676	UGGCUC A GUUUAC	2380	18396	HBV-676 CHz-6 allyl stabl	g ₅ u ₅ a ₅ g ₅ a ₅ c cUGAuGagggccgguuagggccGaa	10868
683	GUUUAC U AGUGCC	2381	18397	HBV-683 CHz-6 allyl stabl	g ₅ g ₅ c ₅ g ₅ a ₅ cu cUGAuGagggccgguuagggccGaa	10869
1150	UUUACC C CGUUGC	2382	18402	HBV-1150 CHz-6 allyl stabl	g ₅ c ₅ a ₅ g ₅ a ₅ c ₅ g cUGAuGagggccgguuagggccGaa	10870
1200	GCAACC C CCACUG	2383	18403	HBV-1200 CHz-6 allyl stabl	c ₅ a ₅ g ₅ u ₅ g ₅ g cUGAuGagggccgguuagggccGaa	10871
1201	CAACCC C CACUGG	2384	18404	HBV-1201 CHz-6 allyl stabl	c ₅ g ₅ a ₅ g ₅ g ₅ u ₅ g cUGAuGagggccgguuagggccGaa	10872
1444	CGGCGC U GAAUCC	2385	18405	HBV-1444 CHz-6 allyl stabl	g ₅ g ₅ a ₅ u ₅ g ₅ uc cUGAuGagggccgguuagggccGaa	10873
1451	GAAUCC C GCGGAC	2386	18406	HBV-1451 CHz-6 allyl stabl	g ₅ u ₅ c ₅ g ₅ c ₅ g ₅ c cUGAuGagggccgguuagggccGaa	10874
1533	CGCACC U CUCUUU	2387	18407	HBV-1533 CHz-6 allyl stabl	a ₅ g ₅ a ₅ g ₅ g ₅ ag cUGAuGagggccgguuagggccGaa	10875
1600	CACCUC U GCACGU	2388	18410	HBV-1600 CHz-6 allyl stabl	a ₅ c ₅ g ₅ u ₅ g ₅ c cUGAuGagggccgguuagggccGaa	10876
1698	CCGACC U UGAGGC	2389	18411	HBV-1698 CHz-6 allyl stabl	g ₅ c ₅ g ₅ c ₅ u ₅ g ₅ ca cUGAuGagggccgguuagggccGaa	10877
1784	GGAGGC U GUAGGC	2390	18412	HBV-1784 CHz-6 allyl stabl	g ₅ c ₅ c ₅ u ₅ g ₅ ac cUGAuGagggccgguuagggccGaa	10878
1829	UUUUUC A CCUCUG	2391	18414	HBV-1829 CHz-6 allyl stabl	c ₅ a ₅ g ₅ a ₅ g ₅ g ₅ g cUGAuGagggccgguuagggccGaa	10879
1876	GCCUCC A AGCUGU	2392	18420	HBV-1876 CHz-6 allyl stabl	a ₅ c ₅ g ₅ a ₅ g ₅ cu cUGAuGagggccgguuagggccGaa	10880
1880	CCAAGC U GUGCCU	2393	18422	HBV-1880 CHz-6 allyl stabl	a ₅ g ₅ g ₅ c ₅ g ₅ ac cUGAuGagggccgguuagggccGaa	10881
218	UUUUUCU U GUUGACA	2394	18333	HBV-218 Rz-7 allyl stabl	u ₅ g ₅ u ₅ c ₅ g ₅ aac cUGAuGagggccgguuagggccGaa	10882
257	CUAGACU C GUGGUGG	2395	18336	HBV-257 Rz-7 allyl stabl	c ₅ g ₅ a ₅ g ₅ c ₅ ac cUGAuGagggccgguuagggccGaa	10883
268	GUGGACU U CUCUCAA	2396	18338	HBV-268 Rz-7 allyl stabl	u ₅ u ₅ g ₅ a ₅ g ₅ ag cUGAuGagggccgguuagggccGaa	10884
269	UGGACUU C UCUCAAU	2397	18339	HBV-269 Rz-7 allyl stabl	a ₅ u ₅ u ₅ g ₅ a ₅ ga cUGAuGagggccgguuagggccGaa	10885
271	GACUUCU C UCAAUUU	2398	18340	HBV-271 Rz-7 allyl stabl	a ₅ a ₅ a ₅ u ₅ g ₅ ga cUGAuGagggccgguuagggccGaa	10886
273	CUUCUCU C AAUUUUC	2399	18341	HBV-273 Rz-7 allyl stabl	g ₅ a ₅ a ₅ a ₅ auu cUGAuGagggccgguuagggccGaa	10887
277	UCUCAU U UUCUAGG	2400	18342	HBV-277 Rz-7 allyl stabl	c ₅ c ₅ u ₅ a ₅ g ₅ aa cUGAuGagggccgguuagggccGaa	10888
278	CUCAAUU U UCUAGGG	2401	18343	HBV-278 Rz-7 allyl stabl	c ₅ c ₅ c ₅ u ₅ g ₅ aga cUGAuGagggccgguuagggccGaa	10889
279	UCAAUUU U CUAGGGG	2402	18344	HBV-279 Rz-7 allyl stabl	c ₅ c ₅ c ₅ g ₅ u ₅ ag cUGAuGagggccgguuagggccGaa	10890
314	CAAAAUU C GCAGUCC	2403	18347	HBV-314 Rz-7 allyl stabl	g ₅ g ₅ a ₅ c ₅ g ₅ uc cUGAuGagggccgguuagggccGaa	10891
385	GAUGUGU C UGCGGGG	2404	18348	HBV-385 Rz-7 allyl stabl	c ₅ g ₅ c ₅ c ₅ g ₅ ga cUGAuGagggccgguuagggccGaa	10892
394	GCGGCGU U UUAUCAU	2405	18349	HBV-394 Rz-7 allyl stabl	a ₅ u ₅ g ₅ a ₅ u ₅ aa cUGAuGagggccgguuagggccGaa	10893
402	UUAUCAU C UUCUCUCU	2406	18352	HBV-402 Rz-7 allyl stabl	a ₅ g ₅ a ₅ g ₅ g ₅ aa cUGAuGagggccgguuagggccGaa	10894
423	UGCUGCU A UGCCUCA	2407	18353	HBV-423 Rz-7 allyl stabl	u ₅ g ₅ a ₅ g ₅ g ₅ ca cUGAuGagggccgguuagggccGaa	10895
429	UAUGCCU C AUCUUCU	2408	18354	HBV-429 Rz-7 allyl stabl	a ₅ g ₅ a ₅ a ₅ g ₅ au cUGAuGagggccgguuagggccGaa	10896
679	GCUCAGU U UACUAGU	2409	18356	HBV-679 Rz-7 allyl stabl	a ₅ c ₅ u ₅ g ₅ a ₅ g ₅ ua cUGAuGagggccgguuagggccGaa	10897

680	CUCAGUU U ACUAGUG	2410	18357	HBV-680 Rz-7 allyl1 stabl	C ₅ A ₅ C ₅ U ₅ agu cUGAuGagggccguuaggccGaa Aacugag B	10898
681	UCAGUUU A CUAGUGC	2411	18358	HBV-681 Rz-7 allyl1 stabl	G ₅ C ₅ A ₅ C ₅ uag cUGAuGagggccguuaggccGaa Aaacuga B	10899
684	GUUACU A GUGCCAU	2412	18359	HBV-684 Rz-7 allyl1 stabl	a ₅ u ₅ g ₅ g ₅ g ₅ cac cUGAuGagggccguuaggccGaa Aguaaac B	10900
692	GUGCCAU U UGUUCAG	2413	18360	HBV-692 Rz-7 allyl1 stabl	C ₅ u ₅ g ₅ A ₅ saca cUGAuGagggccguuaggccGaa Auggcac B	10901
693	UGCCAUU U GUUCAGU	2414	18361	HBV-693 Rz-7 allyl1 stabl	a ₅ g ₅ C ₅ u ₅ g ₅ aac cUGAuGagggccguuaggccGaa Auuggca B	10902
1534	CGCACCU C UCUUUAC	2415	18363	HBV-1534 Rz-7 allyl1 stabl	g ₅ u ₅ s ₅ a ₅ s ₅ aga cUGAuGagggccguuaggccGaa Aggugcg B	10903
1536	CACUCU C UUUACGC	2416	18364	HBV-1536 Rz-7 allyl1 stabl	g ₅ C ₅ g ₅ u ₅ aaa cUGAuGagggccguuaggccGaa Agaggug B	10904
1538	CCUCUCU U UACGCGG	2352	18365	HBV-1538 Rz-7 allyl1 stabl	C ₅ C ₅ g ₅ C ₅ gua cUGAuGagggccguuaggccGaa Agagagg B	10905
1787	AGGUCUG A GGCAUAA	2417	18369	HBV-1787 Rz-7 allyl1 stabl	u ₅ u ₅ s ₅ A ₅ u ₅ gcc cUGAuGagggccguuaggccGaa Acagccu B	10906
1793	UAGGCAU A AAUUGGU	2418	18370	HBV-1793 Rz-7 allyl1 stabl	a ₅ g ₅ C ₅ a ₅ s ₅ auu cUGAuGagggccguuaggccGaa Augccua B	10907
1874	CAAGCCU C CAAGCUG	2419	18372	HBV-1874 Rz-7 allyl1 stabl	C ₅ a ₅ g ₅ C ₅ suug cUGAuGagggccguuaggccGaa Aggcuug B	10908
1887	UGUGCCU U GGUGGGC	2420	18373	HBV-1887 Rz-7 allyl1 stabl	g ₅ C ₅ s ₅ A ₅ s ₅ ccc cUGAuGagggccguuaggccGaa Aggcaca B	10909
2383	AAGAACU C CCUGGCC	2421	18375	HBV-2383 Rz-7 allyl1 stabl	g ₅ g ₅ C ₅ g ₅ g ₅ agg cUGAuGagggccguuaggccGaa Agnuucu B	10910
2828	ACCAUUAU U CUUGGGA	2422	18377	HBV-2828 Rz-7 allyl1 stabl	u ₅ C ₅ C ₅ C ₅ aaag cUGAuGagggccguuaggccGaa Anauggu B	10911
2829	CCAUAUU C UUGGGAA	2423	18378	HBV-2829 Rz-7 allyl1 stabl	u ₅ u ₅ C ₅ C ₅ caa cUGAuGagggccguuaggccGaa Auauggg B	10912
2831	AUAUUU C GGAACA	2424	18380	HBV-2831 Rz-7 allyl1 stabl	u ₅ g ₅ u ₅ u ₅ ccc cUGAuGagggccguuaggccGaa Agaauau B	10913
256	UCUAGAC U CGUGGUG	2425	18381	HBV-256 CHZ-7 allyl1 stabl	C ₅ a ₅ C ₅ C ₅ acg cUGAuGagggccguuaggccGaa Iucuaga B	10914
267	GGUGGAC U UCUCUCA	2426	18382	HBV-267 CHZ-7 allyl1 stabl	u ₅ g ₅ A ₅ g ₅ g ₅ aga cUGAuGagggccguuaggccGaa Iuccacc B	10915
270	GGACUUC U CUCAAUU	2427	18383	HBV-270 CHZ-7 allyl1 stabl	a ₅ a ₅ u ₅ u ₅ g ₅ ag cUGAuGagggccguuaggccGaa Iaagucc B	10916
272	ACUUCUC U CAUUUUU	2428	18384	HBV-272 CHZ-7 allyl1 stabl	a ₅ a ₅ s ₅ A ₅ suug cUGAuGagggccguuaggccGaa Iagaagu B	10917
274	UUCUCUC A AUUUUCU	2429	18385	HBV-274 CHZ-7 allyl1 stabl	a ₅ g ₅ A ₅ A ₅ aa cUGAuGagggccguuaggccGaa Iagagaa B	10918
386	AUGUGUC U GCGGCGU	2430	18386	HBV-386 CHZ-7 allyl1 stabl	a ₅ C ₅ g ₅ C ₅ cgC cUGAuGagggccguuaggccGaa Iacacau B	10919
419	AUCCUGC U GCUAUGC	2431	18387	HBV-419 CHZ-7 allyl1 stabl	g ₅ C ₅ s ₅ u ₅ g ₅ agc cUGAuGagggccguuaggccGaa Icaggau B	10920
422	CUGCUGC U AUGCCUC	2432	18388	HBV-422 CHZ-7 allyl1 stabl	g ₅ a ₅ g ₅ g ₅ g ₅ cau cUGAuGagggccguuaggccGaa Icagcag B	10921
427	GCUAUGC C UCAUCUU	2433	18389	HBV-427 CHZ-7 allyl1 stabl	a ₅ a ₅ s ₅ A ₅ suga cUGAuGagggccguuaggccGaa Icauagc B	10922
428	CUAUGCC U CAUCUUC	2434	18390	HBV-428 CHZ-7 allyl1 stabl	g ₅ a ₅ g ₅ g ₅ aug cUGAuGagggccguuaggccGaa Igcauag B	10923
430	AUGCCUC A UCUUCUU	2435	18392	HBV-430 CHZ-7 allyl1 stabl	a ₅ a ₅ s ₅ A ₅ aga cUGAuGagggccguuaggccGaa Iaggcau B	10924
608	UGUAUUC C CAUCCCA	2436	18393	HBV-608 CHZ-7 allyl1 stabl	u ₅ g ₅ g ₅ g ₅ aug cUGAuGagggccguuaggccGaa Iaaucac B	10925
609	GUUAUCC C AUCCCAU	2437	18394	HBV-609 CHZ-7 allyl1 stabl	a ₅ u ₅ g ₅ g ₅ g ₅ au cUGAuGagggccguuaggccGaa Igaauac B	10926
669	GUUUCUC U UGGCUCU	2438	18395	HBV-669 CHZ-7 allyl1 stabl	u ₅ g ₅ A ₅ g ₅ scca cUGAuGagggccguuaggccGaa Iagaacac B	10927
689	CUAUGGC C AUUUGUU	2439	18398	HBV-689 CHZ-7 allyl1 stabl	a ₅ a ₅ C ₅ A ₅ aaa cUGAuGagggccguuaggccGaa Icacuag B	10928
690	UAGUGCC A UUUUGUUC	2440	18399	HBV-690 CHZ-7 allyl1 stabl	g ₅ a ₅ s ₅ C ₅ aaa cUGAuGagggccguuaggccGaa Igcacua B	10929
718	GCUUUCC C CCACUGU	2441	18400	HBV-718 CHZ-7 allyl1 stabl	a ₅ C ₅ A ₅ g ₅ u ₅ g cUGAuGagggccguuaggccGaa Igaagac B	10930
1149	CCUUUAC C CCGUUGC	2442	18401	HBV-1149 CHZ-7 allyl1 stabl	g ₅ C ₅ A ₅ A ₅ cg ₅ cUGAuGagggccguuaggccGaa Iuaaagg B	10931

1535	GCACCUC U CUUUACG	2443	18408	HBV-1535	CHz-7 allyl stabl	c ₅ s ₅ u ₅ a ₅ aag	cUGAuGagggccg ₅ uuaggccGaa	Iaggugc B	10932
1537	ACCUCUC U UUACGG	2444	18409	HBV-1537	CHz-7 allyl stabl	c ₅ s ₅ c ₅ s ₅ uaa	cUGAuGagggccg ₅ uuaggccGaa	Iagaggu B	10933
1791	UGUAGGC A UAAAUUG	2445	18413	HBV-1791	CHz-7 allyl stabl	c ₅ a ₅ a ₅ u ₅ uaa	cUGAuGagggccg ₅ uuaggccGaa	Iccuaca B	10934
1831	UUUUCAC C UCUGCCU	2446	18415	HBV-1831	CHz-7 allyl stabl	a ₅ s ₅ s ₅ c ₅ aga	cUGAuGagggccg ₅ uuaggccGaa	Iugaaaa B	10935
1832	UUUCACC U CUGCCUA	2447	18416	HBV-1832	CHz-7 allyl stabl	u ₅ a ₅ s ₅ s ₅ cag	cUGAuGagggccg ₅ uuaggccGaa	Igugaaa B	10936
1872	UUCAAAG C UCCAAGC	2448	18417	HBV-1872	CHz-7 allyl stabl	g ₅ c ₅ u ₅ s ₅ gga	cUGAuGagggccg ₅ uuaggccGaa	Icuugaa B	10937
1873	UCAAGCC U CCAAGCU	2449	18418	HBV-1873	CHz-7 allyl stabl	a ₅ s ₅ c ₅ u ₅ u ₅ g	cUGAuGagggccg ₅ uuaggccGaa	Igcunga B	10938
1875	AAGCCUC C AAGCUGU	2450	18419	HBV-1875	CHz-7 allyl stabl	a ₅ c ₅ a ₅ s ₅ gcu	cUGAuGagggccg ₅ uuaggccGaa	Iagggcu B	10939
1876	AGCCUCC A AGCUGUG	2451	18421	HBV-1876	CHz-7 allyl stabl	c ₅ a ₅ c ₅ a ₅ gcu	cUGAuGagggccg ₅ uuaggccGaa	Igaggu B	10940
1880	UCCAAGC U GUGCCUU	2452	18423	HBV-1880	CHz-7 allyl stabl	a ₅ a ₅ s ₅ s ₅ cac	cUGAuGagggccg ₅ uuaggccGaa	Icuugga B	10941
2382	GAAGAAC U CCCUCGC	2453	18424	HBV-2382	CHz-7 allyl stabl	g ₅ c ₅ s ₅ a ₅ s ₅ ggg	cUGAuGagggccg ₅ uuaggccGaa	Iuucuu B	10942
2384	AGAACUC C CUCGCCU	2454	18425	HBV-2384	CHz-7 allyl stabl	a ₅ s ₅ s ₅ c ₅ gag	cUGAuGagggccg ₅ uuaggccGaa	Iaguucu B	10943
2385	GAACUCC C UCGCCUC	2455	18426	HBV-2385	CHz-7 allyl stabl	g ₅ a ₅ s ₅ s ₅ cga	cUGAuGagggccg ₅ uuaggccGaa	Igaguuc B	10944
2422	GGGUCGC A GAAGAUC	2456	18427	HBV-2422	CHz-7 allyl stabl	g ₅ a ₅ u ₅ c ₅ uuc	cUGAuGagggccg ₅ uuaggccGaa	Icgacgc B	10945
2830	CAUAUUC U UGGGAAC	2457	18428	HBV-2830	CHz-7 allyl stabl	g ₅ u ₅ u ₅ c ₅ cca	cUGAuGagggccg ₅ uuaggccGaa	Iaauaug B	10946
234	AAUCCU C ACAUA	2363	19179	HBV-234	Rz-6 amino stabl	u ₅ a ₅ u ₅ u ₅ ggu	cUGAuGagggccg ₅ uuaggccGaa	Aggaau B	10947
252	GAGUCU A GACUCG	2364	19180	HBV-252	Rz-6 amino stabl	c ₅ s ₅ a ₅ s ₅ guc	cUGAuGagggccg ₅ uuaggccGaa	Agacuc B	10948
268	UGGACU U CUCUCA	2365	19182	HBV-268	Rz-6 amino stabl	u ₅ s ₅ a ₅ s ₅ gag	cUGAuGagggccg ₅ uuaggccGaa	Agucca B	10949
280	AAUUU C UAGGGG	2366	19190	HBV-280	Rz-6 amino stabl	c ₅ c ₅ c ₅ c ₅ ua	cUGAuGagggccg ₅ uuaggccGaa	Aaaau B	10950
313	CAAAU U CGCAGU	2367	19191	HBV-313	Rz-6 amino stabl	a ₅ c ₅ u ₅ g ₅ c ₅ g	cUGAuGagggccg ₅ uuaggccGaa	Auuuug B	10951
395	GGCGUU U UAUCAU	2368	19195	HBV-395	Rz-6 amino stabl	a ₅ u ₅ g ₅ a ₅ ua	cUGAuGagggccg ₅ uuaggccGaa	Aacgcc B	10952
402	UAUCAU C UUCCUC	2369	19196	HBV-402	Rz-6 amino stabl	g ₅ a ₅ s ₅ s ₅ gaa	cUGAuGagggccg ₅ uuaggccGaa	Augaua B	10953
607	UGUAUU C CCAUCC	2370	19200	HBV-607	Rz-6 amino stabl	g ₅ s ₅ a ₅ u ₅ gg	cUGAuGagggccg ₅ uuaggccGaa	Aauaca B	10954
697	UUUGUU C AGUGGU	2371	19207	HBV-697	Rz-6 amino stabl	a ₅ c ₅ c ₅ a ₅ scu	cUGAuGagggccg ₅ uuaggccGaa	Aacaaa B	10955
1539	UCUCUU U ACGCGG	2372	19211	HBV-1539	Rz-6 amino stabl	c ₅ c ₅ g ₅ c ₅ gu	cUGAuGagggccg ₅ uuaggccGaa	Aagaga B	10956
1599	UCACCU C UGCACG	2373	19212	HBV-1599	Rz-6 amino stabl	c ₅ s ₅ u ₅ g ₅ ca	cUGAuGagggccg ₅ uuaggccGaa	Agguga B	10957
1607	GCACGU C GCAUGG	2374	19213	HBV-1607	Rz-6 amino stabl	c ₅ c ₅ a ₅ u ₅ g ₅ c	cUGAuGagggccg ₅ uuaggccGaa	Acgugc B	10958
1833	UCACCU C UGCCUA	2375	19216	HBV-1833	Rz-6 amino stabl	u ₅ a ₅ s ₅ s ₅ gca	cUGAuGagggccg ₅ uuaggccGaa	Agguga B	10959
2383	AGAAU C CCUCGC	2376	19219	HBV-2383	Rz-6 amino stabl	g ₅ c ₅ s ₅ a ₅ gg	cUGAuGagggccg ₅ uuaggccGaa	Aguucu B	10960
2429	GAAGAU C UCAAUC	2377	19221	HBV-2429	Rz-6 amino stabl	g ₅ a ₅ u ₅ u ₅ gga	cUGAuGagggccg ₅ uuaggccGaa	Aucuuc B	10961
2831	UAUTUC U GGGAAC	2378	19224	HBV-2831	Rz-6 amino stabl	g ₅ u ₅ u ₅ c ₅ gcc	cUGAuGagggccg ₅ uuaggccGaa	Agaaua B	10962
430	UGCCUC A UCUCUC	2379	19236	HBV-430	CHz-6 amino stabl	a ₅ g ₅ a ₅ a ₅ ga	cUGAuGagggccg ₅ uuaggccGaa	Iaggca B	10963
676	UGGCUC A GUUUAC	2380	19241	HBV-676	CHz-6 amino stabl	g ₅ u ₅ a ₅ a ₅ ac	cUGAuGagggccg ₅ uuaggccGaa	Iagcca B	10964
683	GUUUAC U AGUGCC	2381	19242	HBV-683	CHz-6 amino stabl	g ₅ s ₅ c ₅ a ₅ cu	cUGAuGagggccg ₅ uuaggccGaa	Iuaaac B	10965

1150	UUUACC C CGUUGC	2382	19247	HBV-1150 CHz-6 amino stabl	g ₆ c ₆ a ₆ a ₆ c ₆ g	cUGAUGagggccguuagggccGaa	Iguaaa B	10966
1200	GCAACC C CCACUG	2383	19248	HBV-1200 CHz-6 amino stabl	c ₆ a ₆ g ₆ u ₆ g ₆ g	cUGAUGagggccguuagggccGaa	Iguugc B	10967
1201	CAACCC C CACUGG	2384	19249	HBV-1201 CHz-6 amino stabl	c ₆ c ₆ a ₆ g ₆ g ₆ u ₆ g	cUGAUGagggccguuagggccGaa	Igguu ₆ B	10968
1444	CGCGCG U GAAUCC	2385	19250	HBV-1444 CHz-6 amino stabl	g ₆ g ₆ a ₆ u ₆ g ₆ uc	cUGAUGagggccguuagggccGaa	Icgccg B	10969
1451	GAAUCC C GCGGAC	2386	19251	HBV-1451 CHz-6 amino stabl	g ₆ u ₆ c ₆ g ₆ g ₆ c	cUGAUGagggccguuagggccGaa	Igaau ₆ B	10970
1533	CGCACC U CUCUUU	2387	19252	HBV-1533 CHz-6 amino stabl	a ₆ g ₆ a ₆ g ₆ g ₆ ag	cUGAUGagggccguuagggccGaa	Igu ₆ cg B	10971
1600	CACCUC U GCACGU	2388	19255	HBV-1600 CHz-6 amino stabl	a ₆ c ₆ g ₆ u ₆ g ₆ gc	cUGAUGagggccguuagggccGaa	Iaggu ₆ B	10972
1698	CCGACC U UGAGGC	2389	19256	HBV-1698 CHz-6 amino stabl	g ₆ c ₆ c ₆ u ₆ g ₆ ca	cUGAUGagggccguuagggccGaa	Igucg ₆ B	10973
1784	GGAGGC U GUAGGC	2390	19257	HBV-1784 CHz-6 amino stabl	g ₆ c ₆ c ₆ u ₆ g ₆ ac	cUGAUGagggccguuagggccGaa	Iccucc B	10974
1829	UUUUUC A CCUCUG	2391	19259	HBV-1829 CHz-6 amino stabl	c ₆ a ₆ g ₆ a ₆ g ₆ g	cUGAUGagggccguuagggccGaa	Iaaaa ₆ B	10975
1876	GCCUCC A AGCUGU	2392	19265	HBV-1876 CHz-6 amino stabl	a ₆ c ₆ a ₆ g ₆ g ₆ cu	cUGAUGagggccguuagggccGaa	Igaggg B	10976
1880	CCAAGC U GUGCCU	2393	19267	HBV-1880 CHz-6 amino stabl	a ₆ g ₆ g ₆ c ₆ g ₆ ac	cUGAUGagggccguuagggccGaa	Icuug ₆ B	10977
218	UUUUUC U GUUGACA	2394	19178	HBV-218 Rz-7 amino stabl	u ₆ g ₆ u ₆ c ₆ g ₆ aac	cUGAUGagggccguuagggccGaa	Agaaaa B	10978
257	CUAGACU C GUGGUG	2395	19181	HBV-257 Rz-7 amino stabl	c ₆ c ₆ a ₆ c ₆ g ₆ ac	cUGAUGagggccguuagggccGaa	Agucua ₆ g B	10979
268	GUGGACU U CUCUCAA	2396	19183	HBV-268 Rz-7 amino stabl	u ₆ u ₆ g ₆ a ₆ g ₆ ag	cUGAUGagggccguuagggccGaa	Aguccac B	10980
269	UGGACUU C UCUCAAU	2397	19184	HBV-269 Rz-7 amino stabl	a ₆ u ₆ u ₆ g ₆ g ₆ aga	cUGAUGagggccguuagggccGaa	Aagucca B	10981
271	GACUUUC C UCAAUUU	2398	19185	HBV-271 Rz-7 amino stabl	a ₆ a ₆ a ₆ u ₆ u ₆ ga	cUGAUGagggccguuagggccGaa	Agaaguc B	10982
273	CUUCUCU C AAUUUUC	2399	19186	HBV-273 Rz-7 amino stabl	g ₆ a ₆ a ₆ g ₆ auu	cUGAUGagggccguuagggccGaa	Agagaag B	10983
277	UCUCAAU U UUCUAGG	2400	19187	HBV-277 Rz-7 amino stabl	c ₆ c ₆ u ₆ g ₆ a ₆ gaa	cUGAUGagggccguuagggccGaa	Auugaga B	10984
278	CUCAAUU U UCUAGGG	2401	19188	HBV-278 Rz-7 amino stabl	c ₆ c ₆ c ₆ u ₆ g ₆ aga	cUGAUGagggccguuagggccGaa	Aauugag B	10985
279	UCAAUUU U CUAGGGG	2402	19189	HBV-279 Rz-7 amino stabl	c ₆ c ₆ c ₆ g ₆ u ₆ ag	cUGAUGagggccguuagggccGaa	Aaauga B	10986
314	CAAAUU C GCAGUCC	2403	19192	HBV-314 Rz-7 amino stabl	g ₆ g ₆ a ₆ c ₆ g ₆ uc	cUGAUGagggccguuagggccGaa	Aauuug B	10987
385	GAUGUGU C UGCGGCG	2404	19193	HBV-385 Rz-7 amino stabl	c ₆ g ₆ c ₆ g ₆ g ₆ ca	cUGAUGagggccguuagggccGaa	Acacauc B	10988
394	GCGGCGU U UUAUCAU	2405	19194	HBV-394 Rz-7 amino stabl	a ₆ u ₆ g ₆ a ₆ g ₆ uaa	cUGAUGagggccguuagggccGaa	Acgccgc B	10989
402	UUAUCAU C UUCUCUC	2406	19197	HBV-402 Rz-7 amino stabl	a ₆ g ₆ a ₆ g ₆ g ₆ gaa	cUGAUGagggccguuagggccGaa	Augauaa B	10990
423	UGCUGCU A UGCCUCA	2407	19198	HBV-423 Rz-7 amino stabl	u ₆ g ₆ a ₆ g ₆ g ₆ gca	cUGAUGagggccguuagggccGaa	Agcagca B	10991
429	UAUGCCU C AUCUUCU	2408	19199	HBV-429 Rz-7 amino stabl	a ₆ g ₆ a ₆ g ₆ g ₆ gau	cUGAUGagggccguuagggccGaa	Aggcaua B	10992
679	GCUCAGU U UACUAGU	2409	19201	HBV-679 Rz-7 amino stabl	a ₆ c ₆ u ₆ a ₆ g ₆ g ₆ ua	cUGAUGagggccguuagggccGaa	Acugagc B	10993
680	CUCAGUU U ACUAGUG	2410	19202	HBV-680 Rz-7 amino stabl	c ₆ a ₆ c ₆ u ₆ g ₆ agu	cUGAUGagggccguuagggccGaa	Aacugag B	10994
681	UCAGUUU A CUAGUGC	2411	19203	HBV-681 Rz-7 amino stabl	g ₆ c ₆ a ₆ g ₆ c ₆ uag	cUGAUGagggccguuagggccGaa	Aaacuga B	10995
684	GUUUACU A GUGCCAU	2412	19204	HBV-684 Rz-7 amino stabl	a ₆ u ₆ g ₆ g ₆ g ₆ cac	cUGAUGagggccguuagggccGaa	Aguaaac B	10996
692	GUGCCAU U UGUUCAG	2413	19205	HBV-692 Rz-7 amino stabl	c ₆ u ₆ g ₆ a ₆ g ₆ aca	cUGAUGagggccguuagggccGaa	Auggcac B	10997
693	UGCCAUU U GUUCAGU	2414	19206	HBV-693 Rz-7 amino stabl	a ₆ c ₆ u ₆ g ₆ g ₆ aac	cUGAUGagggccguuagggccGaa	Aauggca B	10998
1534	CGCACC C UCUUUAC	2415	19208	HBV-1534 Rz-7 amino stabl	g ₆ u ₆ a ₆ g ₆ a ₆ ga	cUGAUGagggccguuagggccGaa	Aggu ₆ cg B	10999

1536	CACCUCU C UUUACGC	2416	19209	HBV-1536 Rz-7 amino stabl	G ₆ C ₆ G ₆ U ₆ aaa cUGAU/GagggccgguuaggccGaa Agaggug B	11000
1538	CCUCUCU U UACGGG	2352	19210	HBV-1538 Rz-7 amino stabl	C ₆ S ₆ G ₆ C ₆ gua cUGAU/GagggccgguuaggccGaa Agagg B	11001
1787	AGGCUGU A GGCAUAA	2417	19214	HBV-1787 Rz-7 amino stabl	U ₆ U ₆ A ₆ U ₆ ggcc cUGAU/GagggccgguuaggccGaa Acagccu B	11002
1793	UAGGCAU A AAUUGGU	2418	19215	HBV-1793 Rz-7 amino stabl	A ₆ S ₆ C ₆ A ₆ uuu cUGAU/GagggccgguuaggccGaa Augccua B	11003
1874	CAAGCCU C CAAGCUG	2419	19217	HBV-1874 Rz-7 amino stabl	C ₆ A ₆ G ₆ C ₆ uuu cUGAU/GagggccgguuaggccGaa Aggcuug B	11004
1887	UGUGCCU U GGGUGG	2420	19218	HBV-1887 Rz-7 amino stabl	G ₆ C ₆ C ₆ A ₆ ccc cUGAU/GagggccgguuaggccGaa Aggcaca B	11005
2383	AAGAACU C CCUCGCC	2421	19220	HBV-2383 Rz-7 amino stabl	G ₆ G ₆ C ₆ G ₆ agg cUGAU/GagggccgguuaggccGaa Aguucuu B	11006
2828	ACCAUUA U CUUGGGA	2422	19222	HBV-2828 Rz-7 amino stabl	U ₆ C ₆ C ₆ A ₆ ag cUGAU/GagggccgguuaggccGaa Auauugu B	11007
2829	CCAUAUU C UUGGGAA	2423	19223	HBV-2829 Rz-7 amino stabl	U ₆ U ₆ C ₆ C ₆ caa cUGAU/GagggccgguuaggccGaa Auauugg B	11008
2831	AUAUUCU U GGGAACA	2424	19225	HBV-2831 Rz-7 amino stabl	U ₆ G ₆ U ₆ U ₆ ccc cUGAU/GagggccgguuaggccGaa AGaaauu B	11009
256	UCUAGAC U CGUGGUG	2425	19226	HBV-256 CHz-7 amino stabl	C ₆ A ₆ C ₆ C ₆ acg cUGAU/GagggccgguuaggccGaa Iucuaga B	11010
267	GGUGGAC U UCUCUCA	2426	19227	HBV-267 CHz-7 amino stabl	U ₆ G ₆ A ₆ G ₆ aga cUGAU/GagggccgguuaggccGaa Iuccacc B	11011
270	GGACUUC U CUCAAUU	2427	19228	HBV-270 CHz-7 amino stabl	A ₆ S ₆ U ₆ U ₆ gag cUGAU/GagggccgguuaggccGaa Iaaqucc B	11012
272	ACUUCUC U CAUUUUU	2428	19229	HBV-272 CHz-7 amino stabl	A ₆ S ₆ A ₆ U ₆ uug cUGAU/GagggccgguuaggccGaa Iagaagu B	11013
274	UUCUCUC A AUUUUCU	2429	19230	HBV-274 CHz-7 amino stabl	A ₆ G ₆ A ₆ A ₆ auu cUGAU/GagggccgguuaggccGaa Iagagaa B	11014
386	AUGUGUC U GCGGCGU	2430	19231	HBV-386 CHz-7 amino stabl	A ₆ C ₆ G ₆ C ₆ gpc cUGAU/GagggccgguuaggccGaa Iacacau B	11015
419	AUCCUGC U GCUAUGC	2431	19232	HBV-419 CHz-7 amino stabl	G ₆ S ₆ A ₆ U ₆ agc cUGAU/GagggccgguuaggccGaa Iaggauu B	11016
422	CUGCUGC U AUGCCUC	2432	19233	HBV-422 CHz-7 amino stabl	G ₆ A ₆ G ₆ G ₆ cau cUGAU/GagggccgguuaggccGaa Iagcgag B	11017
427	GCUAUGC C UCAUCUU	2433	19234	HBV-427 CHz-7 amino stabl	A ₆ A ₆ S ₆ A ₆ uga cUGAU/GagggccgguuaggccGaa Icauagc B	11018
428	CUAUGCC U CAUCUUC	2434	19235	HBV-428 CHz-7 amino stabl	G ₆ A ₆ S ₆ G ₆ aug cUGAU/GagggccgguuaggccGaa Igcauag B	11019
430	AUGCCUC A UCUUCUU	2435	19237	HBV-430 CHz-7 amino stabl	A ₆ A ₆ S ₆ A ₆ aga cUGAU/GagggccgguuaggccGaa Iaggcau B	11020
608	UGUAUUC C CAUCCCA	2436	19238	HBV-608 CHz-7 amino stabl	U ₆ G ₆ G ₆ G ₆ aug cUGAU/GagggccgguuaggccGaa Iaaauca B	11021
609	GUUAUCC C AUCCCAU	2437	19239	HBV-609 CHz-7 amino stabl	A ₆ U ₆ S ₆ G ₆ ggu cUGAU/GagggccgguuaggccGaa Igaauac B	11022
669	GUUUCUC U UGGCUCA	2438	19240	HBV-669 CHz-7 amino stabl	U ₆ G ₆ A ₆ G ₆ cca cUGAU/GagggccgguuaggccGaa Iagaaac B	11023
689	CUAGUGC C AUUUGUU	2439	19243	HBV-689 CHz-7 amino stabl	A ₆ A ₆ C ₆ A ₆ auu cUGAU/GagggccgguuaggccGaa Icacuag B	11024
690	UAGUGCC A UUUUGUUC	2440	19244	HBV-690 CHz-7 amino stabl	G ₆ A ₆ A ₆ C ₆ aaa cUGAU/GagggccgguuaggccGaa Igcaqua B	11025
718	GUUUUCC C CCACUGU	2441	19245	HBV-718 CHz-7 amino stabl	A ₆ C ₆ A ₆ G ₆ ugg cUGAU/GagggccgguuaggccGaa Igaaagc B	11026
1149	CCUUUAC C CCGUUGC	2442	19246	HBV-1149 CHz-7 amino stabl	G ₆ C ₆ A ₆ A ₆ cgg cUGAU/GagggccgguuaggccGaa Iuaaagg B	11027
1535	GCACCUC U CUUUACG	2443	19253	HBV-1535 CHz-7 amino stabl	C ₆ G ₆ U ₆ A ₆ aaag cUGAU/GagggccgguuaggccGaa Iaggugc B	11028
1537	ACCUCUC U UUAACGG	2444	19254	HBV-1537 CHz-7 amino stabl	C ₆ G ₆ C ₆ G ₆ uaa cUGAU/GagggccgguuaggccGaa Iagaggu B	11029
1791	UGUAGGC A UAAUUG	2445	19258	HBV-1791 CHz-7 amino stabl	C ₆ A ₆ A ₆ U ₆ uaa cUGAU/GagggccgguuaggccGaa Iccuaca B	11030
1831	UUUUCAC C UCUGCCU	2446	19260	HBV-1831 CHz-7 amino stabl	A ₆ G ₆ G ₆ C ₆ aga cUGAU/GagggccgguuaggccGaa Iugaaaa B	11031
1832	UUUCACC U CUGCCUA	2447	19261	HBV-1832 CHz-7 amino stabl	U ₆ A ₆ G ₆ G ₆ cag cUGAU/GagggccgguuaggccGaa Igugaaa B	11032
1872	UUCAAGC C UCCAAGC	2448	19262	HBV-1872 CHz-7 amino stabl	G ₆ C ₆ U ₆ U ₆ gga cUGAU/GagggccgguuaggccGaa Icuugaa B	11033

1873	UCAAAGCC U CCAAGCU	2449	19263	HBV-1873 CHz-7 amino stabl	a ₉ s ₉ c ₉ u ₉ g ₉ cUGAU/GagggcgguuaggccGaa Igcuu ₉ ga B	11034
1875	AAGCCUC C AAGCUGU	2450	19264	HBV-1875 CHz-7 amino stabl	a ₉ c ₉ a ₉ s ₉ cuu cUGAU/GagggcgguuaggccGaa Iaggcuu B	11035
1876	AGCCUCC A AGCUGUG	2451	19266	HBV-1876 CHz-7 amino stabl	c ₉ a ₉ c ₉ a ₉ s ₉ gcu cUGAU/GagggcgguuaggccGaa Iaggguu B	11036
1880	UCCAAGC U GUGCCUU	2452	19268	HBV-1880 CHz-7 amino stabl	a ₉ a ₉ s ₉ s ₉ cac cUGAU/GagggcgguuaggccGaa Icuugga B	11037
2382	GAAGAAC U CCCUCGC	2453	19269	HBV-2382 CHz-7 amino stabl	g ₉ c ₉ s ₉ a ₉ g ₉ g ₉ g ₉ g ₉ cUGAU/GagggcgguuaggccGaa Iuuucuuc B	11038
2384	AGAACUC C CUCGCCU	2454	19270	HBV-2384 CHz-7 amino stabl	a ₉ s ₉ s ₉ a ₉ c ₉ gag cUGAU/GagggcgguuaggccGaa Iaguucu B	11039
2385	GAACUCC C UCGCCUC	2455	19271	HBV-2385 CHz-7 amino stabl	g ₉ a ₉ s ₉ s ₉ cga cUGAU/GagggcgguuaggccGaa Igaguuc B	11040
2422	GCGUCGC A GAAGAUC	2456	19272	HBV-2422 CHz-7 amino stabl	g ₉ a ₉ u ₉ c ₉ uuc cUGAU/GagggcgguuaggccGaa Icagcgc B	11041
2830	CAUAUUC U UGGGAAC	2457	19273	HBV-2830 CHz-7 amino stabl	g ₉ u ₉ s ₉ u ₉ c ₉ cca cUGAU/GagggcgguuaggccGaa Iaauaug B	11042
315	GCCAAAUUC G CAGUC	2458	20079	HBV-315 GCl.Rz-5/10 stab2	g ₉ a ₉ c ₉ g ₉ uGAU ₉ g gcauGcacuaugc gcg gaauuuuggc B	11043
381	AUCGUUGGAU G UGUUCU	2459	20080	HBV-381 GCl.Rz-5/10 stab2	a ₉ s ₉ a ₉ a ₉ uGAU ₉ g gcauGcacuaugc gcg auccagcgau B	11044
476	UUGCOCGUTU G UCCUC	2460	20081	HBV-476 GCl.Rz-5/10 stab2	g ₉ a ₉ s ₉ a uGAU ₉ g gcauGcacuaugc gcg aaacggggcaa B	11045
694	AGUGCCAUIIU G UUCAG	2461	20082	HBV-694 GCl.Rz-5/10 stab2	c ₉ u ₉ s ₉ a uGAU ₉ g gcauGcacuaugc gcg aaauggcacu B	11046
1265	CUCCUCUGCC G AUCCA	2462	20083	HBV-1265 GCl.Rz-5/10 stab2	u ₉ g ₉ s ₉ u uGAU ₉ g gcauGcacuaugc gcg ggagagaggag B	11047
1601	CUUCACCUCU G CACGU	2463	20084	HBV-1601 GCl.Rz-5/10 stab2	a ₉ c ₉ s ₉ s ₉ g uGAU ₉ g gcauGcacuaugc gcg agagggugaag B	11048
1881	CCUCCRAGCU G UGCCU	2464	20085	HBV-1881 GCl.Rz-5/10 stab2	a ₉ s ₉ g ₉ a uGAU ₉ g gcauGcacuaugc gcg agcuuggagg B	11049
1883	UCCAAGCUGU G CCUUG	2465	20086	HBV-1883 GCl.Rz-5/10 stab2	c ₉ a ₉ a ₉ g uGAU ₉ g gcauGcacuaugc gcg acagcuugga B	11050
2388	GAACUCCUC G CCUCG	2466	20087	HBV-2388 GCl.Rz-5/10 stab2	c ₉ g ₉ a ₉ g uGAU ₉ g gcauGcacuaugc gcg gagggagauc B	11051
381	GCUGGAU G UGUCUCG	2467	20091	HBV-381 Zin.Rz-7 amino stab2	g ₉ s ₉ a ₉ s ₉ aca GcccgaagGCGaGugaGGuCu auccagc B	11052
392	CUGCGGC G UUUUAUC	2468	20092	HBV-392 Zin.Rz-7 amino stab2	g ₉ a ₉ u ₉ a ₉ aaa GccgaaagGCGaGugaGGuCu gccgcag B	11053
420	UCCUGCU G CUAUGCC	2469	20093	HBV-420 Zin.Rz-7 amino stab2	g ₉ s ₉ c ₉ a ₉ uag GcccgaagGCGaGugaGGuCu agcagga B	11054
648	UAUGGGA G UGGGCCU	2470	20094	HBV-648 Zin.Rz-7 amino stab2	a ₉ s ₉ g ₉ c ₉ cca GcccgaagGCGaGugaGGuCu uocccaua B	11055
711	UCGUAGG G CUUUCCT	2471	20095	HBV-711 Zin.Rz-7 amino stab2	g ₉ s ₉ g ₉ a ₉ aag GcccgaagGCGaGugaGGuCu ccuacga B	11056
1262	CUCCUCU G CCGAUCC	2472	20096	HBV-1262 Zin.Rz-7 amino stab2	g ₉ s ₉ a ₉ u ₉ c ₉ g GcccgaagGCGaGugaGGuCu agaggag B	11057
1835	CACCUCU G CCTAAUC	2473	20097	HBV-1835 Zin.Rz-7 amino stab2	g ₉ a ₉ u ₉ u ₉ agg GcccgaagGCGaGugaGGuCu agaggug B	11058
2388	CUCCCCUC G CCUCGCA	2474	20098	HBV-2388 Zin.Rz-7 amino stab2	u ₉ s ₉ c ₉ g ₉ agg GcccgaagGCGaGugaGGuCu gagggag B	11059
192	GACCCCU G CUCGUGU	2475	20099	HBV-192 Zin.Rz-7 amino stab2	a ₉ c ₉ a ₉ c ₉ gag GcccgaagGCGaGugaGGuCu agggguc B	11060
198	UGCUCGU G UUACAGG	2476	20100	HBV-198 Zin.Rz-7 amino stab2	c ₉ c ₉ u ₉ g ₉ uaa GcccgaagGCGaGugaGGuCu acgagca B	11061

315	AAAAUUC G CAGUCCC	2477	20101	HBV-315 Zin.Rz-7 stab2	amino	g ₅ g ₅ g ₅ a ₅ cug GccgaaagGCGaGugaGGuCu gaauuuu B	11062
383	GGAUGU G UCUGCG	2478	20102	HBV-383 Zin.Rz-6 stab2	amino	c ₅ g ₅ c ₅ a ₅ ga GccgaaagGCGaGugaGGuCu acaucc B	11063
383	UGGAUGU G UCUGCGG	2479	20103	HBV-383 Zin.Rz-7 stab2	amino	c ₅ c ₅ g ₅ c ₅ aga GccgaaagGCGaGugaGGuCu acaucca B	11064
387	GUGUCU G CGGCGU	2480	20104	HBV-387 Zin.Rz-6 stab2	amino	a ₅ c ₅ g ₅ c ₅ cg GccgaaagGCGaGugaGGuCu agacac B	11065
390	GUCUGCG G CGUUUA	2481	20105	HBV-390 Zin.Rz-7 stab2	amino	u ₅ a ₅ c ₅ a ₅ acg GccgaaagGCGaGugaGGuCu cgcagac B	11066
392	UGCGGC G UUUUAU	2482	20106	HBV-392 Zin.Rz-6 stab2	amino	a ₅ u ₅ a ₅ a ₅ aa GccgaaagGCGaGugaGGuCu gccgca B	11067
425	UGCUAU G CCUCAU	2483	20107	HBV-425 Zin.Rz-6 stab2	amino	a ₅ u ₅ g ₅ a ₅ gg GccgaaagGCGaGugaGGuCu auagca B	11068
425	CUGCUAU G CCUCAUC	2484	20108	HBV-425 Zin.Rz-7 stab2	amino	g ₅ a ₅ u ₅ g ₅ agg GccgaaagGCGaGugaGGuCu auagcag B	11069
468	GUAUGUU G CCGUUU	2485	20109	HBV-468 Zin.Rz-7 stab2	amino	a ₅ a ₅ c ₅ g ₅ ggg GccgaaagGCGaGugaGGuCu aacauac B	11070
476	CCCGUUU G UCCUCUA	2486	20110	HBV-476 Zin.Rz-7 stab2	amino	u ₅ a ₅ g ₅ a ₅ sgga GccgaaagGCGaGugaGGuCu aaacggg B	11071
648	AUGGGA G UGGGCC	2487	20111	HBV-648 Zin.Rz-6 stab2	amino	g ₅ g ₅ c ₅ c ₅ ca GccgaaagGCGaGugaGGuCu ucccau B	11072
694	GCCAUUU G UUCAGUG	2488	20112	HBV-694 Zin.Rz-7 stab2	amino	c ₅ a ₅ c ₅ u ₅ gaa GccgaaagGCGaGugaGGuCu aauggc B	11073
699	UUGUUA G UGGUUCG	2489	20113	HBV-699 Zin.Rz-7 stab2	amino	c ₅ g ₅ a ₅ a ₅ cca GccgaaagGCGaGugaGGuCu ugaacaa B	11074
1262	UCCUCU G CGGAUC	2490	20114	HBV-1262 Zin.Rz-6 stab2	amino	g ₅ a ₅ u ₅ c ₅ gg GccgaaagGCGaGugaGGuCu agagga B	11075
1440	CCGUCG G CGCUGAA	2491	20115	HBV-1440 Zin.Rz-7 stab2	amino	u ₅ u ₅ c ₅ a ₅ gcg GccgaaagGCGaGugaGGuCu cgacggg B	11076
1526	CACGGG G CGCACC	2492	20116	HBV-1526 Zin.Rz-6 stab2	amino	g ₅ g ₅ u ₅ g ₅ cg GccgaaagGCGaGugaGGuCu cccgug B	11077
1526	CCAGGG G CGCACCU	2493	20117	HBV-1526 Zin.Rz-7 stab2	amino	a ₅ g ₅ g ₅ u ₅ gcg GccgaaagGCGaGugaGGuCu cccgugg B	11078
1557	CCGUCU G UGCCUUC	2494	20118	HBV-1557 Zin.Rz-7 stab2	amino	g ₅ a ₅ g ₅ g ₅ gca GccgaaagGCGaGugaGGuCu agacggg B	11079
1559	CGUCUGU G CCUUCUC	2495	20119	HBV-1559 Zin.Rz-7 stab2	amino	g ₅ a ₅ g ₅ a ₅ agg GccgaaagGCGaGugaGGuCu acagacg B	11080
1590	GCACUUC G CUUCACC	2496	20120	HBV-1590 Zin.Rz-7 stab2	amino	g ₅ g ₅ u ₅ g ₅ saag GccgaaagGCGaGugaGGuCu gaagugc B	11081
1835	ACCUCU G CCUAAU	2497	20121	HBV-1835 Zin.Rz-6 stab2	amino	a ₅ u ₅ u ₅ a ₅ sgg GccgaaagGCGaGugaGGuCu agaggu B	11082
2311	ACCAAAU G CCCCUAU	2498	20122	HBV-2311 Zin.Rz-7 stab2	amino	a ₅ u ₅ a ₅ g ₅ ggg GccgaaagGCGaGugaGGuCu auuuggu B	11083

2420	CCGCGUC G CAGAAGA	2499	20123	HBV-2420 Zin.Rz-7 stab2	amino	u _g c _s ^u _g ^u _g cug GccgaaaagGCGaGugaGGuCu gacgcgg B	11084
65	CCUGCUG G UGGCUCC	2500	20124	HBV-65 Zin.Rz-7 stab2	amino	g _s g _s a _s g _s cca GccgaaaagGCGaGugaGGuCu cagcagg B	11085
192	ACCCCU G CUCGUG	2501	20125	HBV-192 Zin.Rz-6 stab2	amino	c _s a _s c _s g _s ag GccgaaaagGCGaGugaGGuCu aggggu B	11086
198	GCUCGU G UUACAG	2502	20126	HBV-198 Zin.Rz-6 stab2	amino	c _g ^u _g g _s ^u _g aa GccgaaaagGCGaGugaGGuCu acgagc B	11087
258	UAGACUC G UGGUGGA	2503	20127	HBV-258 Zin.Rz-7 stab2	amino	u _g c _s a _s a _s cca GccgaaaagGCGaGugaGGuCu gagucua B	11088
261	ACUCGUG G UGGACUU	2504	20128	HBV-261 Zin.Rz-7 stab2	amino	a _g a _s g _s ^u _g cca GccgaaaagGCGaGugaGGuCu cagcagu B	11089
315	AAAUUC G CAGUCC	2505	20129	HBV-315 Zin.Rz-6 stab2	amino	g _s g _s a _s c _s ug GccgaaaagGCGaGugaGGuCu gaauuu B	11090
381	CUGGAU G UGUCUG	2506	20130	HBV-381 Zin.Rz-6 stab2	amino	c _s a _s g _s a _s ca GccgaaaagGCGaGugaGGuCu auccag B	11091
387	UGUGUCU G CGGCGUU	2507	20131	HBV-387 Zin.Rz-7 stab2	amino	a _g a _s c _s g _s ccg GccgaaaagGCGaGugaGGuCu agacaca B	11092
390	UCUGCG G CGUUUU	2508	20132	HBV-390 Zin.Rz-6 stab2	amino	a _g a _s a _s a _s c _g GccgaaaagGCGaGugaGGuCu cgcaga B	11093
417	CAUCCU G CUGCUA	2509	20133	HBV-417 Zin.Rz-6 stab2	amino	u _g a _s g _s c _s ag GccgaaaagGCGaGugaGGuCu aggaug B	11094
420	CCUGCU G CUAUGC	2510	20134	HBV-420 Zin.Rz-6 stab2	amino	g _s c _s a _s u _g ag GccgaaaagGCGaGugaGGuCu agcagg B	11095
468	UAUGUU G CCCGUU	2511	20135	HBV-468 Zin.Rz-6 stab2	amino	a _g a _s c _s g _s gg GccgaaaagGCGaGugaGGuCu aacaua B	11096
476	CCGUUU G UCCUCU	2512	20136	HBV-476 Zin.Rz-6 stab2	amino	a _g g _s a _s g _s ga GccgaaaagGCGaGugaGGuCu aaacgg B	11097
677	GGCUCA G UUUACU	2513	20137	HBV-677 Zin.Rz-6 stab2	amino	a _g g _s ^u _g a _s aa GccgaaaagGCGaGugaGGuCu ugagcc B	11098
677	UGGCUCA G UUUACUA	2514	20138	HBV-677 Zin.Rz-7 stab2	amino	u _g a _s g _s ^u _g aaa GccgaaaagGCGaGugaGGuCu ugagcca B	11099
685	UUACUA G UGCCAU	2515	20139	HBV-685 Zin.Rz-6 stab2	amino	a _g ^u _g g _s g _s ca GccgaaaagGCGaGugaGGuCu uaguaa B	11100
685	UUUACUA G UGCCAUU	2516	20140	HBV-685 Zin.Rz-7 stab2	amino	a _g a _g ^u _g g _s gca GccgaaaagGCGaGugaGGuCu uaguaaaa B	11101
687	UACUAGU G CCAUUUG	2517	20141	HBV-687 Zin.Rz-7 stab2	amino	c _s a _s a _s a _s ugg GccgaaaagGCGaGugaGGuCu acuagua B	11102
699	UGUUCA G UGGUUC	2518	20142	HBV-699 Zin.Rz-6 stab2	amino	g _s a _s a _s c _s ca GccgaaaagGCGaGugaGGuCu ugaaca B	11103
702	UCAGUG G UUCGUA	2519	20143	HBV-702 Zin.Rz-6 stab2	amino	u _g a _s c _s g _s aa GccgaaaagGCGaGugaGGuCu cacuga B	11104
702	UUCAGUG G UUCGUAG	2520	20144	HBV-702 Zin.Rz-7 stab2	amino	c _g ^u _g a _s c _s gaa GccgaaaagGCGaGugaGGuCu cacugaa B	11105

711	CGUAGG G CUUUC	2521	20145	HBV-711 Zin.Rz-6 stab2	amino	g ₅ g ₅ a ₅ a ₅ ag GccgaaagGCGaGugaGGuCu ccuacg B	11106
1006	UUGUGG G UCUUU	2522	20146	HBV-1006 Zin.Rz-6 stab2	amino	a ₅ a ₅ a ₅ a ₅ ga GccgaaagGCGaGugaGGuCu ccacaa B	11107
1103	UUUCUC G CCAACU	2523	20147	HBV-1103 Zin.Rz-6 stab2	amino	a ₅ g ₅ u ₅ u ₅ gg GccgaaagGCGaGugaGGuCu gagaaa B	11108
1103	CUUCUC G CCAACU	2524	20148	HBV-1103 Zin.Rz-7 stab2	amino	a ₅ a ₅ g ₅ u ₅ gg GccgaaagGCGaGugaGGuCu gagaaag B	11109
1184	GCCAAGU G UUUGCUG	2525	20149	HBV-1184 Zin.Rz-7 stab2	amino	c ₅ a ₅ g ₅ c ₅ aaa GccgaaagGCGaGugaGGuCu acuuggc B	11110
1440	CCGUCG G CGCUGA	2526	20150	HBV-1440 Zin.Rz-6 stab2	amino	u ₅ c ₅ a ₅ g ₅ c ₅ g GccgaaagGCGaGugaGGuCu cgacgg B	11111
1442	GUCGGC G CUGAAU	2527	20151	HBV-1442 Zin.Rz-6 stab2	amino	a ₅ u ₅ u ₅ c ₅ ag GccgaaagGCGaGugaGGuCu gcgac B	11112
1442	CGUCGC G CUGAUC	2528	20152	HBV-1442 Zin.Rz-7 stab2	amino	g ₅ a ₅ u ₅ u ₅ cag GccgaaagGCGaGugaGGuCu gccgacg B	11113
1553	CUCCCC G UCUGUG	2529	20153	HBV-1553 Zin.Rz-6 stab2	amino	c ₅ a ₅ c ₅ a ₅ ga GccgaaagGCGaGugaGGuCu ggggag B	11114
1557	CCGUCU G UGCCUU	2530	20154	HBV-1557 Zin.Rz-6 stab2	amino	a ₅ a ₅ g ₅ g ₅ ca GccgaaagGCGaGugaGGuCu agacgg B	11115
1559	GUCUGU G CCUUCU	2531	20155	HBV-1559 Zin.Rz-6 stab2	amino	a ₅ g ₅ a ₅ a ₅ gg GccgaaagGCGaGugaGGuCu acagac B	11116
1583	CCGUGU G CACUUC	2532	20156	HBV-1583 Zin.Rz-6 stab2	amino	g ₅ a ₅ a ₅ g ₅ ug GccgaaagGCGaGugaGGuCu acacgg B	11117
1590	CACUUC G CUUCAC	2533	20157	HBV-1590 Zin.Rz-6 stab2	amino	g ₅ u ₅ g ₅ a ₅ ag GccgaaagGCGaGugaGGuCu gaagug B	11118
1622	ACCACC G UGAACG	2534	20158	HBV-1622 Zin.Rz-6 stab2	amino	c ₅ g ₅ u ₅ u ₅ ca GccgaaagGCGaGugaGGuCu gguggu B	11119
1870	UGUCAA G CCUCCAA	2535	20159	HBV-1870 Zin.Rz-7 stab2	amino	u ₅ u ₅ g ₅ g ₅ agg GccgaaagGCGaGugaGGuCu uugaaca B	11120
1881	CCAAGCU G UGCCUUG	2536	20160	HBV-1881 Zin.Rz-7 stab2	amino	c ₅ a ₅ c ₅ g ₅ g ₅ ca GccgaaagGCGaGugaGGuCu agcuugg B	11121
1883	AGCUGU G CCUUGG	2537	20161	HBV-1883 Zin.Rz-6 stab2	amino	c ₅ c ₅ a ₅ a ₅ gg GccgaaagGCGaGugaGGuCu acagcu B	11122
1883	AAGCUGU G CCUUGGG	2538	20162	HBV-1883 Zin.Rz-7 stab2	amino	c ₅ c ₅ a ₅ a ₅ gg GccgaaagGCGaGugaGGuCu acagcuu B	11123
2311	CCAAAU G CCCCUA	2539	20163	HBV-2311 Zin.Rz-6 stab2	amino	u ₅ a ₅ g ₅ g ₅ gg GccgaaagGCGaGugaGGuCu auuugg B	11124
2347	ACUGUU G UUAGAC	2540	20164	HBV-2347 Zin.Rz-6 stab2	amino	g ₅ u ₅ c ₅ u ₅ aa GccgaaagGCGaGugaGGuCu aacagu B	11125
2364	AGGCAG G UCCCCU	2541	20165	HBV-2364 Zin.Rz-6 stab2	amino	a ₅ g ₅ g ₅ g ₅ ga GccgaaagGCGaGugaGGuCu cugccu B	11126
2364	GAGGCAG G UCCCCUA	2542	20166	HBV-2364 Zin.Rz-7 stab2	amino	u ₅ a ₅ g ₅ g ₅ gga GccgaaagGCGaGugaGGuCu cugccuc B	11127

2388	UCCUC G CCUCG	2543	20167	HBV-2388 Zin.Rz-6 stab2	amino	G _S ³ G _S ⁴ G _S ⁵ G _S ⁶ G _S ⁷ G _S ⁸ G _S ⁹ G _S ¹⁰ G _S ¹¹ G _S ¹² G _S ¹³ G _S ¹⁴ G _S ¹⁵ G _S ¹⁶ G _S ¹⁷ G _S ¹⁸ G _S ¹⁹ G _S ²⁰ G _S ²¹ G _S ²² G _S ²³ G _S ²⁴ G _S ²⁵ G _S ²⁶ G _S ²⁷ G _S ²⁸ G _S ²⁹ G _S ³⁰ G _S ³¹ G _S ³² G _S ³³ G _S ³⁴ G _S ³⁵ G _S ³⁶ G _S ³⁷ G _S ³⁸ G _S ³⁹ G _S ⁴⁰ G _S ⁴¹ G _S ⁴² G _S ⁴³ G _S ⁴⁴ G _S ⁴⁵ G _S ⁴⁶ G _S ⁴⁷ G _S ⁴⁸ G _S ⁴⁹ G _S ⁵⁰ G _S ⁵¹ G _S ⁵² G _S ⁵³ G _S ⁵⁴ G _S ⁵⁵ G _S ⁵⁶ G _S ⁵⁷ G _S ⁵⁸ G _S ⁵⁹ G _S ⁶⁰ G _S ⁶¹ G _S ⁶² G _S ⁶³ G _S ⁶⁴ G _S ⁶⁵ G _S ⁶⁶ G _S ⁶⁷ G _S ⁶⁸ G _S ⁶⁹ G _S ⁷⁰ G _S ⁷¹ G _S ⁷² G _S ⁷³ G _S ⁷⁴ G _S ⁷⁵ G _S ⁷⁶ G _S ⁷⁷ G _S ⁷⁸ G _S ⁷⁹ G _S ⁸⁰ G _S ⁸¹ G _S ⁸² G _S ⁸³ G _S ⁸⁴ G _S ⁸⁵ G _S ⁸⁶ G _S ⁸⁷ G _S ⁸⁸ G _S ⁸⁹ G _S ⁹⁰ G _S ⁹¹ G _S ⁹² G _S ⁹³ G _S ⁹⁴ G _S ⁹⁵ G _S ⁹⁶ G _S ⁹⁷ G _S ⁹⁸ G _S ⁹⁹ G _S ¹⁰⁰ G _S ¹⁰¹ G _S ¹⁰² G _S ¹⁰³ G _S ¹⁰⁴ G _S ¹⁰⁵ G _S ¹⁰⁶ G _S ¹⁰⁷ G _S ¹⁰⁸ G _S ¹⁰⁹ G _S ¹¹⁰ G _S ¹¹¹ G _S ¹¹² G _S ¹¹³ G _S ¹¹⁴ G _S ¹¹⁵ G _S ¹¹⁶ G _S ¹¹⁷ G _S ¹¹⁸ G _S ¹¹⁹ G _S ¹²⁰ G _S ¹²¹ G _S ¹²² G _S ¹²³ G _S ¹²⁴ G _S ¹²⁵ G _S ¹²⁶ G _S ¹²⁷ G _S ¹²⁸ G _S ¹²⁹ G _S ¹³⁰ G _S ¹³¹ G _S ¹³² G _S ¹³³ G _S ¹³⁴ G _S ¹³⁵ G _S ¹³⁶ G _S ¹³⁷ G _S ¹³⁸ G _S ¹³⁹ G _S ¹⁴⁰ G _S ¹⁴¹ G _S ¹⁴² G _S ¹⁴³ G _S ¹⁴⁴ G _S ¹⁴⁵ G _S ¹⁴⁶ G _S ¹⁴⁷ G _S ¹⁴⁸ G _S ¹⁴⁹ G _S ¹⁵⁰ G _S ¹⁵¹ G _S ¹⁵² G _S ¹⁵³ G _S ¹⁵⁴ G _S ¹⁵⁵ G _S ¹⁵⁶ G _S ¹⁵⁷ G _S ¹⁵⁸ G _S ¹⁵⁹ G _S ¹⁶⁰ G _S ¹⁶¹ G _S ¹⁶² G _S ¹⁶³ G _S ¹⁶⁴ G _S ¹⁶⁵ G _S ¹⁶⁶ G _S ¹⁶⁷ G _S ¹⁶⁸ G _S ¹⁶⁹ G _S ¹⁷⁰ G _S ¹⁷¹ G _S ¹⁷² G _S ¹⁷³ G _S ¹⁷⁴ G _S ¹⁷⁵ G _S ¹⁷⁶ G _S ¹⁷⁷ G _S ¹⁷⁸ G _S ¹⁷⁹ G _S ¹⁸⁰ G _S ¹⁸¹ G _S ¹⁸² G _S ¹⁸³ G _S ¹⁸⁴ G _S ¹⁸⁵ G _S ¹⁸⁶ G _S ¹⁸⁷ G _S ¹⁸⁸ G _S ¹⁸⁹ G _S ¹⁹⁰ G _S ¹⁹¹ G _S ¹⁹² G _S ¹⁹³ G _S ¹⁹⁴ G _S ¹⁹⁵ G _S ¹⁹⁶ G _S ¹⁹⁷ G _S ¹⁹⁸ G _S ¹⁹⁹ G _S ²⁰⁰ G _S ²⁰¹ G _S ²⁰² G _S ²⁰³ G _S ²⁰⁴ G _S ²⁰⁵ G _S ²⁰⁶ G _S ²⁰⁷ G _S ²⁰⁸ G _S ²⁰⁹ G _S ²¹⁰ G _S ²¹¹ G _S ²¹² G _S ²¹³ G _S ²¹⁴ G _S ²¹⁵ G _S ²¹⁶ G _S ²¹⁷ G _S ²¹⁸ G _S ²¹⁹ G _S ²²⁰ G _S ²²¹ G _S ²²² G _S ²²³ G _S ²²⁴ G _S ²²⁵ G _S ²²⁶ G _S ²²⁷ G _S ²²⁸ G _S ²²⁹ G _S ²³⁰ G _S ²³¹ G _S ²³² G _S ²³³ G _S ²³⁴ G _S ²³⁵ G _S ²³⁶ G _S ²³⁷ G _S ²³⁸ G _S ²³⁹ G _S ²⁴⁰ G _S ²⁴¹ G _S ²⁴² G _S ²⁴³ G _S ²⁴⁴ G _S ²⁴⁵ G _S ²⁴⁶ G _S ²⁴⁷ G _S ²⁴⁸ G _S ²⁴⁹ G _S ²⁵⁰ G _S ²⁵¹ G _S ²⁵² G _S ²⁵³ G _S ²⁵⁴ G _S ²⁵⁵ G _S ²⁵⁶ G _S ²⁵⁷ G _S ²⁵⁸ G _S ²⁵⁹ G _S ²⁶⁰ G _S ²⁶¹ G _S ²⁶² G _S ²⁶³ G _S ²⁶⁴ G _S ²⁶⁵ G _S ²⁶⁶ G _S ²⁶⁷ G _S ²⁶⁸ G _S ²⁶⁹ G _S ²⁷⁰ G _S ²⁷¹ G _S ²⁷² G _S ²⁷³ G _S ²⁷⁴ G _S ²⁷⁵ G _S ²⁷⁶ G _S ²⁷⁷ G _S ²⁷⁸ G _S ²⁷⁹ G _S ²⁸⁰ G _S ²⁸¹ G _S ²⁸² G _S ²⁸³ G _S ²⁸⁴ G _S ²⁸⁵ G _S ²⁸⁶ G _S ²⁸⁷ G _S ²⁸⁸ G _S ²⁸⁹ G _S ²⁹⁰ G _S ²⁹¹ G _S ²⁹² G _S ²⁹³ G _S ²⁹⁴ G _S ²⁹⁵ G _S ²⁹⁶ G _S ²
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476	CCGUUU G UCCUCU	2512	20198	HBV-476 Amb. Rz-6 stab2	a ₈ g ₈ a ₈ g ₈ gga gga L ucCCUUcaagga L ucCGGG aaacgg B	11159
651	GGGAGUG G GCCUCAG	2564	20199	HBV-651 Amb. Rz-7 stab2	c ₈ u ₈ g ₈ a ₈ gggc gga L ucCCUUcaagga L ucCGGG cacuccc B	11160
677	UGGCUCA G UUUACUA	2514	20200	HBV-677 Amb. Rz-7 stab2	u ₈ a ₈ g ₈ u ₈ gaaa gga L ucCCUUcaagga L ucCGGG ugagcca B	11161
685	UUUACUA G UGCCAUU	2516	20201	HBV-685 Amb. Rz-7 stab2	a ₈ a ₈ u ₈ g ₈ gca gga L ucCCUUcaagga L ucCGGG uaguaaa B	11162
702	UUCAGUG G UUCGUAG	2520	20202	HBV-702 Amb. Rz-7 stab2	c ₈ u ₈ a ₈ c ₈ gaa gga L ucCCUUcaagga L ucCGGG cacugaa B	11163
709	GUUCGUA G GGCUUUC	2565	20203	HBV-709 Amb. Rz-7 stab2	g ₈ a ₈ g ₈ a ₈ gcc gga L ucCCUUcaagga L ucCGGG uacgaac B	11164
710	UCGUAG G GCUUUC	2566	20204	HBV-710 Amb. Rz-6 stab2	g ₈ a ₈ a ₈ g ₈ gc gga L ucCCUUcaagga L ucCGGG cuacga B	11165
747	UAUGGAU G AUGUGGU	2567	20205	HBV-747 Amb. Rz-7 stab2	a ₈ c ₈ c ₈ a ₈ cau gga L ucCCUUcaagga L ucCGGG auccaua B	11166
1557	CCGUUU G UGCCUU	2530	20206	HBV-1557 Amb. Rz-6 stab2	a ₈ a ₈ g ₈ g ₈ ca gga L ucCCUUcaagga L ucCGGG agacgg B	11167
1881	CCAAGCU G UGCCUUG	2536	20207	HBV-1881 Amb. Rz-7 stab2	c ₈ a ₈ a ₈ g ₈ gca gga L ucCCUUcaagga L ucCGGG agcuug B	11168
2347	ACUGUU G UUAGAC	2540	20208	HBV-2347 Amb. Rz-6 stab2	g ₈ u ₈ c ₈ u ₈ gaa gga L ucCCUUcaagga L ucCGGG aacagu B	11169
2375	CUAGAA G AAGAAC	2568	20209	HBV-2375 Amb. Rz-6 stab2	g ₈ u ₈ u ₈ c ₈ uu gga L ucCCUUcaagga L ucCGGG uucuag B	11170
2378	GAAGAA G AACUCC	2569	20210	HBV-2378 Amb. Rz-6 stab2	g ₈ g ₈ a ₈ g ₈ uu gga L ucCCUUcaagga L ucCGGG uucuuc B	11171
2423	CGUCGCA G AAGAUUU	2570	20211	HBV-2423 Amb. Rz-7 stab2	a ₈ g ₈ a ₈ u ₈ cuu gga L ucCCUUcaagga L ucCGGG ugcgacg B	11172
2426	GCAGAA G AUCUCA	2571	20212	HBV-2426 Amb. Rz-6 stab2	u ₈ g ₈ a ₈ g ₈ au gga L ucCCUUcaagga L ucCGGG uucugc B	11173
2426	CGCAGAA G AUCUCAA	2572	20213	HBV-2426 Amb. Rz-7 stab2	u ₈ u ₈ g ₈ a ₈ g ₈ au gga L ucCCUUcaagga L ucCGGG uucugcg B	11174
2476	UAAGGU G GGAAAC	2573	20214	HBV-2476 Amb. Rz-6 stab2	g ₈ u ₈ u ₈ g ₈ cc gga L ucCCUUcaagga L ucCGGG accuua B	11175
2477	UAAGGUG G GAAACUU	2574	20215	HBV-2477 Amb. Rz-7 stab2	a ₈ a ₈ g ₈ g ₈ uuc gga L ucCCUUcaagga L ucCGGG caccuua B	11176
2477	AAGGUG G GAAACU	2575	20216	HBV-2477 Amb. Rz-6 stab2	a ₈ g ₈ u ₈ u ₈ uc gga L ucCCUUcaagga L ucCGGG caccuu B	11177
1607	UGCACGU C GCAUGGA	2576	20697	HBV-1607 Rz-7 allyl stab1 (7/4)	u ₈ c ₈ c ₈ a ₈ g ₈ ugc cUGAuGagggccguuagggccGaa Acgugca B	11178
1887	GUGCCU U GGGUGG	2577	20698	HBV-1887 Rz-6 allyl stab1 (6/4)	c ₈ c ₈ a ₈ c ₈ cc cUGAuGagggccguuagggccGaa Aggcac B	11179
1607	GCACGU C GCAUGG	2374	20699	HBV-1607 Rz-6 allyl stab1 (6/3)	c ₈ c ₈ a ₈ u ₈ g ₈ gc cUGAuGagggccguuagggccGaa Acgugc B	11180
1607	UGCACGU C GCAUGGA	2576	20700	HBV-1607 Rz-7 allyl stab1 (7/3)	u ₈ c ₈ c ₈ a ₈ g ₈ ugc cUGAuGagggccguuagggccGaa Acgugca B	11181
1887	GUGCCU U GGGUGG	2577	20701	HBV-1887 Rz-6 allyl stab1 (6/3)	c ₈ c ₈ a ₈ c ₈ cc cUGAuGagggccguuagggccGaa Aggcac B	11182
1887	UGUGCCU U GGGUGGC	2420	20702	HBV-1887 Rz-7 allyl stab1 (7/3)	g ₈ c ₈ c ₈ a ₈ g ₈ ccc cUGAuGagggccguuagggccGaa Aggcaca B	11183
313	CCAAAU U CGCAGUC	2346	22798	HBV-313 Rz-7 Ome stab1	gacugcg CUGAuGagggccguuagggccGAA Anuuug B	11184
408	UCUUCU C UGCAUCC	2349	22799	HBV-408 Rz-7 Ome stab1	ggaugca CUGAuGagggccguuagggccGAA Aggaaga B	11185
1756	AGGAGGU U AGGUACA	2353	22800	HBV-1756 Rz-7 Ome stab1	uuuacuu CUGAuGagggccguuagggccGAA Accuccu B	11186
10	CUCCACC A CUUCCA	2356	22770	HBV-10 CHz-7 Ome stab1	uggaaag CUGAuGagggccguuagggccGAA Iguggag B	11187
335	UCCAGUC A CUCACCA	2357	22771	HBV-335 CHz-7 Ome stab1	uggugag CUGAuGagggccguuagggccGAA Iacugga B	11188
273	CUUCUCU C AAUUUUC	2399	22645	HBV-273 Rz-7 allyl stab1 (7/3-GUUA)	g ₈ a ₈ a ₈ g ₈ auu cUGAuGagggccguuagggccGaa Agagaag B	11189

273	CUUCUCU C AAUUUUC	2399	22646	HBV-273 Rz-7 allyl stab1 (7/4-GUUA)	g ₈ a ₈ a ₈ a ₈ uuu cUGAUgagggccguuaggccGaa Agagaag B	11190
273	CUUCUCU C AAUUUUC	2399	22648	HBV-273 Rz-7 allyl stab1 (7/3-GAAA)	g ₈ a ₈ a ₈ a ₈ uuu cUGAUgagccgaaaggccGaa Agagaag B	11191
273	CUUCUCU C AAUUUUC	2578	22650	HBV-273 Rz-7 allyl stab1 (7/4-GAAA)	g ₈ a ₈ a ₈ a ₈ uuu cUGAUgagggccgaaaggccGaa Agagaag B	11192
273	UUCUCU C AAUUUU	2578	22644	HBV-273 Rz-6 allyl stab1 (6/3-GUUA)	a ₈ a ₈ a ₈ a ₈ uuu cUGAUgagccguuaggccGaa Agagaa B	11193
273	UUCUCU C AAUUUU	2578	22647	HBV-273 Rz-6 allyl stab1 (6/3-GAAA)	a ₈ a ₈ a ₈ a ₈ uuu cUGAUgagccgaaaggccGaa Agagaa B	11194
273	UUCUCU C AAUUUU	2579	22649	HBV-273 Rz-6 allyl stab1 (6/4-GAAA)	a ₈ a ₈ a ₈ a ₈ uuu cUGAUgagggccgaaaggccGaa Agagaa B	11195
350	ACCUGUU G UCCUCCA	2580	22714	HBV-350 GCl.Rz-7 Stribo stab3	uggagga uGAUg gcauGcacuaugc gCg aacaggu B	11196
1253	CCUUUGU G UCUCUC	2581	22715	HBV-1253 GCl.Rz-7 Stribo stab3	gaggaga uGAUg gcauGcacuaugc gCg acaaagg B	11197
1856	UGUUCAU G UCCUACU	2582	22716	HBV-1856 GCl.Rz-7 Stribo stab3	aguagga uGAUg gcauGcacuaugc gCg augaaca B	11198
1966	GCCUUCU G ACUUCUU	2583	22717	HBV-1966 GCl.Rz-7 Stribo stab3	aagaagu uGAUg gcauGcacuaugc gCg agaaggc B	11199
3132	UCCUCCU G CCUCCAC	2584	22718	HBV-3132 GCl.Rz-7 Stribo stab3	guggagg uGAUg gcauGcacuaugc gCg aggagga B	11200
332	AUCUCCA G UCACUCA	2579	22742	HBV-332 Zin.Rz-7 amino stab4	ugaguga gccgaaaaggGagugagGGuCu uggagau B	11201
350	ACCUGUU G UCCUCCA	2585	22743	HBV-350 Zin.Rz-7 amino stab4	uggagga gccgaaaaggGagugagGGuCu aacaggu B	11202
410	UUCUCUCU G CAUCCUG	2580	22744	HBV-410 Zin.Rz-7 amino stab4	caggaug gccgaaaaggGagugagGGuCu agaggaa B	11203
1253	CCUUUGU G UCUCUC	2586	22745	HBV-1253 Zin.Rz-7 amino stab4	gaggaga gccgaaaaggGagugagGGuCu acaaagg B	11204
1754	GGAGGAG G UUAGGUU	2587	22746	HBV-1754 Zin.Rz-7 amino stab4	aaccuaa gccgaaaaggGagugagGGuCu cuccucc B	11205
407	AUCUUC U CUGCAUC	2588	22772	HBV-407 CHz-7 Ome stab1	gaugcag CUGAUgagggccguuaggccGAA Igaagau B	11206
1848	UCAUCUC A UGUUCAU	2589	22773	HBV-1848 CHz-7 Ome stab1	augaaca CUGAUgagggccguuaggccGAA Igauga B	11207
3124	GCAGCUC C UCCUCCU	2590	22774	HBV-3124 CHz-7 Ome stab1	aggagga CUGAUgagggccguuaggccGAA Iagcugc B	11208
2165	GUCAGCU A UGUCAAC	2591	22801	HBV-2165 Rz-7 Ome stab1	guugaca CUGAUgagggccguuaggccGAA Agcugac B	11209
2706	CCGUAAU A UCCAGAG	2579	22802	HBV-2706 Rz-7 Ome stab1	cucugga CUGAUgagggccguuaggccGAA Auacgg B	11210
350	ACCUGUU G UCCUCCA	2584	22966	HBV-350 Dz-7 stab3	uggagga GGCTAGTACAACGA aacaggu B	11211
332	AUCUCCA G UCACUCA	2592	22967	HBV-332 Dz-7 stab3	ugaguga GGCTAGTACAACGA uggagau B	11212
1840	CUGCCUA A UCAUCUC	2593	22968	HBV-1840 Dz-7 stab3	gagauga GGCTAGTACAACGA uaggcag B	11213
358	UCCUCCA A UUUGUCC	2580	22969	HBV-358 Dz-7 stab3	ggacaaa GGCTAGTACAACGA uggagga B	11214
1253	CCUUUGU G UCUCUC	2346	22970	HBV-1253 Dz-7 stab3 SAC	gaggaga GGCTAGTACAACGA acaaagg B	11215
			20599		c ₈ g ₈ a ₈ u ₈ gu cUAGUgacccgaaaggGaa AagaggB	10834

UPPER CASE = RIBO
UNDERLINE = DEOXY
lower case = 2'-O-methyl
I = inosine
s = phosphorothioate linkage
B = inverted deoxyabasic residue
U = 2'-deoxy-2'-C-allyl Uridine
U = 2'-deoxy-2'-amino Uridine
C = 2'-deoxy-2'-amino Cytidine

Table XII: Group Designation and Dosage levels for HBV transgenic mouse study

Group	Compound	Dose	Number of Mice	Duration of Treatment
1	RPI.18341 (site 273)	100 mg/kg/day*	10F	14 days
2	RPI.18371 (site 1833)	100 mg/kg/day*	10F	14 days
3	RPI.18418 (site 1873)	100 mg/kg/day*	10F	14 days
4	RPI.18372 (site 1874)	100 mg/kg/day*	10F	14 days
5	Saline control	100 mg/kg/day*	10F	14 days
6	Untreated		10F	0 days

*administered via sc infusion using Alzet® mini-osmotic pumps

**TABLE XIII: GROUP DESIGNATION AND DOSAGE LEVELS FOR HBV
TRANSGENIC MOUSE STUDY**

Group	Compound	Dose	Number of Mice	Duration of Treatment
1	RPI.18341 (site 273)	100 mg/kg/day*	15 (M or F)	14 days
2	RPI.18341 (site 273)	30 mg/kg/day*	15 (M or F)	14 days
3	RPI.18341 (site 273)	10 mg/kg/day*	15 (M or F)	14 days
4	RPI.18371 site 1833	100 mg/kg/day*	15 (M or F)	14 days
5	RPI.18371 site 1833	30 mg/kg/day*	15 (M or F)	14 days
6	RPI.18371 site 1833	10 mg/kg/day*	15 (M or F)	14 days
7	SAC (RPI.20599)	100 mg/kg/day*	15 (M or F)	14 days
8	SAC (RPI.20599)	30 mg/kg/day*	15 (M or F)	14 days
9	SAC (RPI.20599)	10 mg/kg/day*	15 (M or F)	14 days
10	Saline control	12 µl/day*	15 (M or F)	14 days
11	3TC® control	50 mg/kg/day, PO	15 (M or F)	14 days

*administered via sc infusion using Alzet® mini-osmotic pumps

Table XIV: HBV RT primer Decoy sequences

Length	Decoy Sequence	Seq ID No.
4	AUUC	11216
4	CAUU	11217
4	UCAU	11218
4	UUCA	11219
5	AUUCA	11220
5	CAUUC	11221
5	UCAUU	11222
5	UUCAU	11223
6	AUUCAU	11224
6	CAUUCA	11225
6	UCAUUC	11226
6	UUCAUU	11227
7	AUUCAUU	11228
7	CAUUCAU	11229
7	UCAUUCA	11230
7	UUCAUUC	11231
8	AUUCAUUC	11232
8	CAUUCAUU	11233
8	UCAUUCAU	11234
8	UUCAUUCA	11235
9	AUUCAUUCA	11236
9	CAUUCAUUC	11237
9	UCAUUCAUU	11238
9	UUCAUUCAU	11239
10	AUUCAUUCAU	11240
10	CAUUCAUUCA	11241
10	UCAUUCAUUC	11242
10	UUCAUUCAUU	11243
11	AUUCAUUCAUU	11244
11	CAUUCAUUCAU	11245
11	UCAUUCAUUCA	11246
11	UUCAUUCAUUC	11247
12	AUUCAUUCAUUC	11248
12	CAUUCAUUCAUU	11249
12	UCAUUCAUUCAU	11250
12	UUCAUUCAUUCA	11251
13	AUUCAUUCAUUCA	11252
13	CAUUCAUUCAUUC	11253
13	UCAUUCAUUCAUU	11254
13	UUCAUUCAUUCAU	11255
14	AUUCAUUCAUUCAU	11256
14	CAUUCAUUCAUUCA	11257
14	UCAUUCAUUCAUUC	11258
14	UUCAUUCAUUCAUU	11259
15	AUUCAUUCAUUCAUU	11260
15	CAUUCAUUCAUUCAU	11261

15	UCAUUCAUUCAUUA	11262
15	UUCAUUCAUUCAUUC	11263
16	AUUCAUUCAUUCAUUC	11264
16	CAUUCAUUCAUUCAU	11265
16	UCAUUCAUUCAUUCAU	11266
16	UUCAUUCAUUCAUUCA	11267
17	AUUCAUUCAUUCAUUA	11268
17	CAUUCAUUCAUUCAUUC	11269
17	UCAUUCAUUCAUUCAU	11270
17	UUCAUUCAUUCAUUCAU	11271
18	AUUCAUUCAUUCAUUAU	11272
18	CAUUCAUUCAUUCAUUA	11273
18	UCAUUCAUUCAUUCAUUC	11274
18	UUCAUUCAUUCAUUCAU	11275
19	AUUCAUUCAUUCAUUAU	11276
19	CAUUCAUUCAUUCAUUAU	11277
19	UCAUUCAUUCAUUCAUUA	11278
19	UUCAUUCAUUCAUUCAUUC	11279
20	AUUCAUUCAUUCAUUAUUC	11280
20	CAUUCAUUCAUUCAUUAU	11281
20	UCAUUCAUUCAUUCAUUAU	11282
20	UUCAUUCAUUCAUUCAUUA	11283
21	AUUCAUUCAUUCAUUAUUA	11284
21	CAUUCAUUCAUUCAUUAUUC	11285
21	UCAUUCAUUCAUUCAUUAU	11286
21	UUCAUUCAUUCAUUCAUUAU	11287
22	CAUUCAUUCAUUCAUUAUUA	11288
22	UCAUUCAUUCAUUCAUUAUUC	11289
22	UUCAUUCAUUCAUUCAUUAU	11290
23	UCAUUCAUUCAUUCAUUAUUA	11291
23	UUCAUUCAUUCAUUCAUUAUUC	11292
24	UUCAUUCAUUCAUUCAUUAUUA	11293

Table XV: Synthetic Nucleic acid molecules

RPI#	Alias	Sequence	SeqID
24961	HBV DR1 2'Oallyl P=S	gscsa _g g _s a _g g _s g _s u _g g _s a _g a _g B	11294
24997	HBV DR1 2'Oallyl P=S control	a _s a _s g _s u _g g _s g _s a _s g _s a _s c _s g _s B	11295
24956	HBV 1866-1869 1x 2'Oallyl P=S	u _s u _s c _s a _s B	11296
24992	HBV 1866-1869 1x 2'Oallyl P=S control	a _s c _s u _s u _s B	11297
24941	HBV 1866-1869 2x 2'Oallyl P=S	u _s u _s c _s a _s u _s u _s c _s a _s B	11298
24959	HBV 1866-1869 2x 2'Oallyl P=S control	a _s c _s u _s u _s a _s c _s u _s u _s B	11299
24944	HBV 1866-1869 3x 2'Oallyl P=S	u _s u _s c _s a _s u _s u _s c _s a _s u _s u _s c _s a _s B	11300
24962	HBV 1866-1869 3x 2'Oallyl P=S control	a _s c _s u _s u _s a _s c _s u _s u _s a _s c _s u _s u _s B	11301
24945	HBV 1866-1869 4x 2'Oallyl P=S	u _s u _s c _s a _s u _s u _s c _s a _s u _s u _s c _s a _s u _s u _s c _s a _s B	11302
24963	HBV 1866-1869 4x 2'Oallyl P=S control	a _s c _s u _s u _s a _s c _s u _s u _s a _s c _s u _s u _s a _s c _s u _s u _s B	11303
24938	HBV 1866-1869 2'Oallyl P=S	u _s g _s a _s a _s B	11304
24974	HBV 1866-1869 2'Oallyl P=S control	a _s a _s g _s u _s B	11305
24940	HBV 1866-1872 2'Oallyl P=S	gscsu _s u _s g _s a _s a _s B	11306
24958	HBV 1866-1872 2'Oallyl P=S control	a _s a _s g _s u _s u _s c _s g _s B	11307
24943	HBV 1866-1876 2'Oallyl P=S	gsgsa _g g _s g _s c _s u _s u _s g _s a _g a _g B	11308
24979	HBV 1866-1876 2'Oallyl P=S control	a _s a _s g _s u _s u _s c _s g _s g _s a _s g _s g _s B	11309
18341	HBV-273 UH.Rz-7 allyl stab1	g _s a _s a _s a _s auu cUGAuGaggccguuaggccGaa Agagaag B	10887
24588	HBV-273 UH.Rz-7 allyl stab1 inact3 scram1 (GUUA SAC)	a _s a _s u _s g _s a _g g cUAGuGacgccguuaggcgGaa Aaugaa B	11310
24929	HBV 1866-1969 2'Omethyl	ugaaB	11311
24965	HBV 1866-1969 2'Omethyl control	aaguB	11312
24934	HBV 1866-1876 2'Omethyl	ggaggcuugaaB	11313
24970	HBV 1866-1876 2'Omethyl control	aaguucggaggB	11314
24976	HBV 1866-1872 2'Omethyl	gcuugaaB	11315
24949	HBV 1866-1872 2'Omethyl control	aaguucgB	11316
24952	HBV DR1 2'Omethyl	gcagaggugaaB	11317
24988	HBV DR1 2'Omethyl control	aaguggagacgB	11318
24947	HBV 1866-1869 1x 2'Omethyl	uucab	11319
24983	HBV 1866-1869 1x 2'Omethyl control	acuuB	11320
24986	HBV 1866-1869 2x 2'Omethyl	uucauucab	11321
24950	HBV 1866-1869 2x 2'Omethyl control	acuuacuuB	11322

24989	HBV 1866-1869 3x 2'Omethyl	uucauucuucaB	11323
24953	HBV 1866-1869 3x 2'Omethyl control	acuuacuacuuB	11324
24936	HBV 1866-1869 4x 2'Omethyl	uucauucuucauucab	11325
24954	HBV 1866-1869 4x 2'Omethyl control	acuuacuacuuacuuB	11326
25639	HBV 5' EnI pos OMe P=S	B u _s u _s u _s c _s u _s a _s a _s g _s u _s a _s a _s c _s a _s g _s u B	11327
25640	HBV 5' EnI neg OMe P=S	B a _s c _s u _s g _s u _s u _s u _s a _s c _s u _s u _s a _s g _s a _s a _s B	11328
25641	HBV 5' EnI sc OMe P=S	B a _s a _s g _s u _s a _s a _s c _s u _s c _s u _s a _s u _s g _s u _s a B	11329
25642	HBV 3' EnI pos OMe P=S	B u _s a _s c _s a _s u _s g _s a _s a _s c _s c _s u _s u _s u _s a _s c _s c _s c _s c _s B	11330
25643	HBV 3' EnI neg OMe P=S	B g _s g _s g _s u _s a _s a _s a _s g _s g _s u _s c _s a _s u _s g _s u _s a B	11331
25644	HBV 3' EnI pos sc OMe P=S	B a _s c _s c _s u _s a _s u _s c _s g _s c _s c _s u _s a _s c _s u _s c _s u _s a _s a B	11332
25645	HBV 5' EnI neg sc OMe P=S	B u _s g _s a _s u _s a _s g _s c _s g _s g _s a _s u _s g _s a _s g _s a _s u _s u B	11333
25646	HBV DR1 pos OMe P=S	B u _s u _s c _s a _s c _s c _s u _s c _s u _s g _s c B	11334
25651	HBV 5' EnI pos Oallyl P=S	B u _s u _s u _s c _s u _s a _s a _s g _s u _s a _s a _s a _s c _s a _s g _s u B	11335
25652	HBV 5' EnI neg Oallyl P=S	B a _s c _s u _s g _s u _s u _s u _s a _s c _s u _s u _s a _s g _s a _s a _s B	11336
25653	HBV 5' EnI sc Oallyl P=S	B a _s a _s g _s u _s a _s a _s c _s u _s c _s u _s a _s u _s g _s u _s a B	11337
25654	HBV 3' EnI pos Oallyl P=S	B u _s a _s c _s a _s u _s g _s a _s a _s c _s c _s u _s u _s u _s a _s c _s c _s c _s c _s B	11338
25655	HBV 3' EnI neg Oallyl P=S	B g _s g _s g _s u _s a _s a _s a _s g _s g _s u _s c _s a _s u _s g _s u _s a B	11339
25656	HBV 3' EnI pos sc Oallyl P=S	B a _s c _s c _s u _s a _s u _s c _s g _s c _s c _s u _s a _s c _s u _s c _s u _s a _s a B	11340
25657	HBV 5' EnI neg sc Oallyl P=S	B u _s g _s a _s u _s a _s g _s c _s g _s g _s a _s u _s g _s a _s g _s a _s u _s u B	11341
25658	HBV DR1 pos Oallyl P=S	B u _s u _s c _s a _s c _s c _s u _s c _s u _s g _s c B	11342

a, g, c, u = all 2'-O-allyl

a, g, c, u = 2'-O-methyl

U= 2'-C-allyl Uridine

S= phosphorothioate

B= inverted deoxybasic

Table XVI: Comparison of Tumor Weight to HBV DNA concentration in mice inoculated with HepG2.2.15 cells

Time point (days)	HBV DNA copies/mL serum	Tumor weight (milligrams)
1	Below detection	No tumor
1	Below detection	No tumor
1	Below detection	No tumor
1	Below detection	No tumor
7	Below detection	No tumor
7	Below detection	No tumor
7	Below detection	No tumor
7	Below detection	No tumor
14	Below detection	No tumor
14	Below detection	No tumor
14	Below detection	No tumor
14	Below detection	No tumor
35	356	33
35	125083	167
35	578	No tumor
35	386	56
42	493	No tumor
42	114431	790
42	94025	359
42	111882	647
49	189885	816
49	Below detection	No tumor
49	293	90
49	41477	2521

Table XVII: Comparison of Tumor Weight to HBV DNA concentration in mice inoculated with G418 resistant HepG2.2.15 cells

Time point (days)	HBV DNA copies/mL serum	Tumor weight (milligrams)
37	7000	1120.0
37	no sample	no sample
37	400000	1962.3
37	26000	558.5
37	380000	2286.0
37	100	317.2
37	52000	1429.0
37	100	427.4
37	26000	813.2
37	1400	631.6
37	186000	1101.5
37	134000	1573.0
37	17800	1040.0
37	16600	1327.2
37	8200	275.7
37	68000	632.8
37	24000	1090.0
37	58000	1082.7
37	12400	1116.3
37	100	763.3

Table XVIII: HCV DNzyme and Substrate Sequence

Pos	Substrate	SEQ ID	DNZYME	SEQ ID
10	UGGGGGCG A CACUCCAC	2594	GTGGAGTG GGCTAGCTACAACGA CGCCCCCA	11343
12	GGGGCGAC A CUCCACCA	2595	TGGTGGAG GGCTAGCTACAACGA GTCGCCCC	11344
17	GACACUCC A CCAUAGAU	2596	ATCTATGG GGCTAGCTACAACGA GGAGTGTC	11345
20	ACUCCACC A UAGAUCAC	2597	GTGATCTA GGCTAGCTACAACGA GGTGGAGT	11346
24	CACCAUAG A UCACUCCC	2598	GGGAGTGA GGCTAGCTACAACGA CTATGGTG	11347
27	CAUAGAUC A CUCCCCUG	2599	CAGGGGAG GGCTAGCTACAACGA GATCTATG	11348
35	ACUCCCCU G UGAGGAAC	2600	GTTCTCTA GGCTAGCTACAACGA AGGGGAGT	11349
42	UGUGAGGA A CUACUGUC	2601	GACAGTAG GGCTAGCTACAACGA TCCTCACA	11350
45	GAGGAACU A CUGUCUUC	2602	GAAGACAG GGCTAGCTACAACGA AGTTCCTC	11351
48	GAACUACU G UCUCACG	2603	CGTGAAGA GGCTAGCTACAACGA AGTAGTTC	11352
54	CUGUCUUC A CGCAGAAA	2604	TTTCTGCG GGCTAGCTACAACGA GAAGACAG	11353
56	GUCUUCAC G CAGAAAGC	2605	GCTTTCTG GGCTAGCTACAACGA GTGAAGAC	11354
63	CGCAGAAA G CGUCUAGC	2606	GCTAGACG GGCTAGCTACAACGA TTTCTGCG	11355
65	CAGAAAGC G UCUAGCCA	2607	TGGCTAGA GGCTAGCTACAACGA GCTTTCTG	11356
70	AGCGUCUA G CCAUGGCG	2608	CGCCATGG GGCTAGCTACAACGA TAGACGCT	11357
73	GUCUAGCC A UGGCGUUA	2609	TAACGCCA GGCTAGCTACAACGA GGCTAGAC	11358
76	UAGCCAUG G CGUUAUA	2610	TACTAACG GGCTAGCTACAACGA CATGGCTA	11359
78	GCCAUGGC G UUAGUAUG	2611	CATACTAA GGCTAGCTACAACGA GCCATGGC	11360
82	UGGCGUUA G UAUGAGUG	2612	CACTCATA GGCTAGCTACAACGA TAACGCCA	11361
84	GCGUUAGU A UGAGUGUC	2613	GACACTCA GGCTAGCTACAACGA ACTAACGC	11362
88	UAGUAUGA G UGUCGUGC	2614	GCACGACA GGCTAGCTACAACGA TCATACTA	11363
90	GUAUGAGU G UCGUGCAG	2615	CTGCACGA GGCTAGCTACAACGA ACTCATAC	11364
93	UGAGUGUC G UGCAGCCU	2616	AGGCTGCA GGCTAGCTACAACGA GACACTCA	11365
95	AGUGUCGU G CAGCCUCC	2617	GGAGGCTG GGCTAGCTACAACGA ACGACACT	11366
98	GUCGUGCA G CCUCCAGG	2618	CCTGGAGG GGCTAGCTACAACGA TGCACGAC	11367
107	CCUCCAGG A CCCCCCU	2619	AGGGGGGG GGCTAGCTACAACGA CCTGGAGG	11368
125	CCGGGAGA G CCAUAGUG	2620	CACATATG GGCTAGCTACAACGA TCTCCCGG	11369
128	GGAGAGCC A UAGUGGUC	2621	GACCACTA GGCTAGCTACAACGA GGCTCTCC	11370
131	GAGCCAU A UGGUCUGC	2622	GCAGACCA GGCTAGCTACAACGA TATGGCTC	11371
134	CCAUAUGG G UCUGCGGA	2623	TCCGCAGA GGCTAGCTACAACGA CACTATGG	11372
138	AGUGGUCU G CGGAACCG	2624	CGGTTCCG GGCTAGCTACAACGA AGACCACT	11373
143	UCUGCGGA A CCGGUGAG	2625	CTCACCGG GGCTAGCTACAACGA TCCGCAGA	11374
147	CGGAACCG G UGAGUACA	2626	TGTACTCA GGCTAGCTACAACGA CGGTTCCG	11375
151	ACCGGUGA G UACACCGG	2627	CCGGTGTA GGCTAGCTACAACGA TCACCGGT	11376
153	CGGUGAGU A CACCGGAA	2628	TTCCGGTG GGCTAGCTACAACGA ACTCACCG	11377
155	GUGAGUAC A CCGGAUU	2629	AATTCCGG GGCTAGCTACAACGA GTACTCAC	11378
161	ACACCGGA A UUGCCAGG	2630	CCTGGCAA GGCTAGCTACAACGA TCCGGTGT	11379
164	CCGGAAUU G CCAGGACG	2631	CGTCCTGG GGCTAGCTACAACGA AATTCCGG	11380
170	UUGCCAGG A CGACCGGG	2632	CCCGGTCG GGCTAGCTACAACGA CCTGGCAA	11381
173	CCAGGACG A CCGGUUCC	2633	GGACCCGG GGCTAGCTACAACGA CGTCCTGG	11382
178	ACGACCGG G UCCUUUCU	2634	AGAAAGGA GGCTAGCTACAACGA CCGGTCGT	11383
190	UUUCUUGG A UCAACCCG	2635	CGGGTTGA GGCTAGCTACAACGA CCAAGAAA	11384
194	UUGGAUCA A CCCGCUCA	2636	TGAGCGGG GGCTAGCTACAACGA TGATCCAA	11385
198	AUCAACCC G CUCAAUGC	2637	GCTATTAG GGCTAGCTACAACGA GGGTTGAT	11386
203	CCCGCUCA A UGCCUGGA	2638	TCCAGGCA GGCTAGCTACAACGA TGAGCGGG	11387
205	CGCUCAAU G CCUGGAGA	2639	TCTCCAGG GGCTAGCTACAACGA ATTGAGCG	11388
213	GCCUGGAG A UUUGGGCG	2640	CGCCCAAA GGCTAGCTACAACGA CTCCAGGC	11389
219	AGAUUUGG G CGUGCCCC	2641	GGGGCACG GGCTAGCTACAACGA CCAAATCT	11390
221	AUUUGGGG G UGCCCCCG	2642	CGGGGGCA GGCTAGCTACAACGA GCCCAAAT	11391
223	UUGGGCGU G CCCCCGCG	2643	CGCGGGGG GGCTAGCTACAACGA ACGCCCAA	11392

229	GUGCCCC G CGAGACUG	2644	CAGTCTCG GGCTAGCTACAACGA GGGGGCAC	11393
234	CCCGCGAG A CUGCUAGC	2645	GCTAGCAG GGCTAGCTACAACGA CTCGCGGG	11394
237	GCGAGACU G CUAGCCGA	2646	TCGGCTAG GGCTAGCTACAACGA AGTCTCGC	11395
241	GACUGCUA G CCGAGUAG	2647	CTACTCGG GGCTAGCTACAACGA TAGCAGTC	11396
246	CUAGCCGA G UAGUGUUG	2648	CAACACTA GGCTAGCTACAACGA TCGGCTAG	11397
249	GCCGAGUA G UGUUGGGU	2649	ACCCAACA GGCTAGCTACAACGA TACTCGGC	11398
251	CGAGUAGU G UUGGGUCG	2650	CGACCCAA GGCTAGCTACAACGA ACTACTCG	11399
256	AGUGUUGG G UCGCGAAA	2651	TTTCGCGA GGCTAGCTACAACGA CCAACACT	11400
259	GUUGGGUC G CGAAAGGC	2652	GCCTTTCG GGCTAGCTACAACGA GACCCAAC	11401
266	CGCGAAAG G CCUUGUGG	2653	CCACAAGG GGCTAGCTACAACGA CTTTCGCG	11402
271	AAGGCCUU G UGUUACUG	2654	CAGTACCA GGCTAGCTACAACGA AAGGCCTT	11403
274	GCCUUGUG G UACUGCCU	2655	AGGCAGTA GGCTAGCTACAACGA CACAAGGC	11404
276	CUUGUGGU A CUGCCUGA	2656	TCAGGCAG GGCTAGCTACAACGA ACCACAAG	11405
279	GUGGUACU G CCUGAUAG	2657	CTATCAGG GGCTAGCTACAACGA AGTACCAC	11406
284	ACUGCCUG A UAGGGUGC	2658	GCACCCTA GGCTAGCTACAACGA CAGGCAGT	11407
289	CUGAUAGG G UGCUUGCG	2659	CGCAAGCA GGCTAGCTACAACGA CCTATCAG	11408
291	GAUAGGGU G CUUGCGAG	2660	CTCGCAAG GGCTAGCTACAACGA ACCCTATC	11409
295	GGGUGCUU G CGAGUGCC	2661	GGCACTCG GGCTAGCTACAACGA AAGCACCC	11410
299	GCUUGCGA G UGCCCCGG	2662	CCGGGGCA GGCTAGCTACAACGA TCGCAAGC	11411
301	UUGCGAGU G CCCCGGGA	2663	TCCCGGGG GGCTAGCTACAACGA ACTCGCAA	11412
311	CCCGGGAG G UCUCGUAG	2664	CTACGAGA GGCTAGCTACAACGA CTCCCGGG	11413
316	GAGGUCUC G UAGACCGU	2665	ACGGTCTA GGCTAGCTACAACGA GAGACCTC	11414
320	UCUCGUAG A CCUGGCAC	2666	GTGCACGG GGCTAGCTACAACGA CTACGAGA	11415
323	CGUAGACC G UGCACCAU	2667	ATGGTGCA GGCTAGCTACAACGA GGTCTACG	11416
325	UAGACCGU G CACCAUGA	2668	TCATGGTG GGCTAGCTACAACGA ACGGTCTA	11417
327	GACCGUGC A CCAUGAGC	2669	GCTCATGG GGCTAGCTACAACGA GCACGGTC	11418
330	CGUGCACC A UGAGCACG	2670	CGTGCTCA GGCTAGCTACAACGA GGTGCACG	11419
334	CACCAUGA G CACGAAUC	2671	GATTCTGT GGCTAGCTACAACGA TCATGGTG	11420
336	CCAUGAGC A CGAAUCCU	2672	AGGATTCT GGCTAGCTACAACGA GCTCATGG	11421
340	GAGCACGA A UCUAAAC	2673	GTTTAGGA GGCTAGCTACAACGA TCGTGCTC	11422
347	AAUCCUAA A CCUCAAG	2674	CTTTGAGG GGCTAGCTACAACGA TTAGGATT	11423
360	AAAGAAA A CCAAACGU	2675	ACGTTTGG GGCTAGCTACAACGA TTTTCTTT	11424
365	AAAACCAA A CGUAAAC	2676	GTGTTACG GGCTAGCTACAACGA TTGGTTTT	11425
367	AACCAAAC G UAACACCA	2677	TGGTGTTA GGCTAGCTACAACGA GTTTGGTT	11426
370	CAAACGUA A CACCAACC	2678	GGTTGGTG GGCTAGCTACAACGA TACGTTTG	11427
372	AACGUAA A CCAACCGC	2679	GCGGTTGG GGCTAGCTACAACGA GTTACGTT	11428
376	UAACACCA A CCGCCGCC	2680	GGCGCGGG GGCTAGCTACAACGA TGGTGTTA	11429
379	CACCAACC G CCGCCAC	2681	GTGGGCGG GGCTAGCTACAACGA GGTGGTGG	11430
382	CAACCGCC G CCACAGG	2682	CCTGTGGG GGCTAGCTACAACGA GCGGTTG	11431
386	CGCCGCC A CAGGACGU	2683	ACGTCTGT GGCTAGCTACAACGA GGGCGGCG	11432
391	CCCACAGG A CGUCAAGU	2684	ACTTGACG GGCTAGCTACAACGA CCTGTGGG	11433
393	CACAGGAC G UCAAGUUC	2685	GAACCTGA GGCTAGCTACAACGA GTCCTGTG	11434
398	GACGUCAA G UUCCCGGG	2686	CCCGGGAA GGCTAGCTACAACGA TTGACGTC	11435
406	GUUCCCGG G CGGUGGUC	2687	GACCACCG GGCTAGCTACAACGA CCGGGAAC	11436
409	CCCGGGCG G UGUUCAGA	2688	TCTGACCA GGCTAGCTACAACGA CGCCCGGG	11437
412	GGGCGGUG G UCAGAUCG	2689	CGATCTGA GGCTAGCTACAACGA CACCGCCC	11438
417	GUGGUCAG A UCGUUGGU	2690	ACCAACGA GGCTAGCTACAACGA CTGACCAC	11439
420	GUCAGAU C G UUGGUGGA	2691	TCCACCAA GGCTAGCTACAACGA GATCTGAC	11440
424	GAUCGUUG G UGGAGUUU	2692	AAACTCCA GGCTAGCTACAACGA CAACGATC	11441
429	UUGGUGGA G UUUACCG	2693	CAGGTAAA GGCTAGCTACAACGA TCCACCAA	11442
433	UGGAGUUU A CCUGUUGC	2694	GCAACAGG GGCTAGCTACAACGA AAATCCA	11443
437	GUUUACCU G UUGCCGCG	2695	CGCGGCAA GGCTAGCTACAACGA AGGTAAAC	11444
440	UACCGUUU G CCGCGCAG	2696	CTGCGCGG GGCTAGCTACAACGA AACAGGTA	11445
443	CUGUUGCC G CGCAGGGG	2697	CCCCGCGG GGCTAGCTACAACGA GGCAACAG	11446
445	GUUGCCCG G CAGGGGCC	2698	GGCCCCGT GGCTAGCTACAACGA GCGGCAAC	11447
451	GCGCAGGG G CCCCAGGU	2699	ACCTGGGG GGCTAGCTACAACGA CCCTGCGC	11448

458	GGCCCCAG G UUGGGUGU	2700	ACACCCAA GGCTAGCTACAACGA CTGGGGCC	11449
463	CAGGUUGG G UGUGCGCG	2701	CGCGCACA GGCTAGCTACAACGA CCAACCTG	11450
465	GGUUGGGU G UGCGCGCG	2702	CGCGCGCA GGCTAGCTACAACGA ACCCAACC	11451
467	UUGGGUGU G CGCGCGAC	2703	GTCGCGCG GGCTAGCTACAACGA ACACCCAA	11452
469	GGGUGUGC G CGCGACUA	2704	TAGTCGCG GGCTAGCTACAACGA GCACACCC	11453
471	GUGUGCGC G CGACUAGG	2705	CCTAGTCG GGCTAGCTACAACGA GCGCACAC	11454
474	UGCGCGCG A CUAGGAAG	2706	CTTCCTAG GGCTAGCTACAACGA CGCGCGCA	11455
483	CUAGGAAG A CUUCCGAG	2707	CTCGGAAG GGCTAGCTACAACGA CTTCCTAG	11456
491	ACUUCCGA G CGGUCGCA	2708	TGCGACCG GGCTAGCTACAACGA TCGGAAGT	11457
494	UCCGAGCG G UCGCAACC	2709	GGTTGCGA GGCTAGCTACAACGA CGCTCGGA	11458
497	GAGCGGUC G CAACCUCG	2710	CGAGGTTG GGCTAGCTACAACGA GACCGCTC	11459
500	CGGUCGCA A CCUCGUGG	2711	CCACGAGG GGCTAGCTACAACGA TGCGACCG	11460
505	GCAACCUC G UGGAAGGC	2712	GCCTTCCA GGCTAGCTACAACGA GAGGTTGC	11461
512	CGUGGAAG G CGACAACC	2713	GGTTGTCT GGCTAGCTACAACGA CTTCACG	11462
515	GGAAGGCG A CAACCUAU	2714	ATAGGTTG GGCTAGCTACAACGA CGCCTTCC	11463
518	AGGCGACA A CCUAUCCC	2715	GGGATAGG GGCTAGCTACAACGA TGTCGCCT	11464
522	GACAACCU A UCCCCAAG	2716	CTTGGGGA GGCTAGCTACAACGA AGGTTGTC	11465
531	UCCCCAAG G CUCGCCGG	2717	CCGGCGAG GGCTAGCTACAACGA CTTGGGGA	11466
535	CAAGGCU C CCGGCCCG	2718	CGGGCCGG GGCTAGCTACAACGA GAGCCTTG	11467
539	GCUCGCCG G CCGGAGGG	2719	CCCTCGGG GGCTAGCTACAACGA CGGCGAGC	11468
547	GCCCCAGG G CAGGGCCU	2720	AGGCCTTG GGCTAGCTACAACGA CCTCGGGC	11469
552	AGGGCAGG G CCUGGGCU	2721	AGCCCAGG GGCTAGCTACAACGA CCTGCCCT	11470
558	GGGCCUGG G CUCAGCCC	2722	GGGCTGAG GGCTAGCTACAACGA CCAGGCCC	11471
563	UGGGCUCA G CCCGGGUA	2723	TACCCGGG GGCTAGCTACAACGA TGAGCCCA	11472
569	CAGCCCGG G UACCCUUG	2724	CAAGGGTA GGCTAGCTACAACGA CCGGGCTG	11473
571	GCCCCGGU A CCCUUGGC	2725	GCCAAGGG GGCTAGCTACAACGA ACCCGGGC	11474
578	UACCCUUG G CCCUCUA	2726	TAGAGGGG GGCTAGCTACAACGA CAAGGGTA	11475
586	GCCCCUCU A UGGCAUUG	2727	CATTGCCA GGCTAGCTACAACGA AGAGGGGC	11476
589	CCUCUAUG G CAAUGAGG	2728	CCTCATTG GGCTAGCTACAACGA CATAGAGG	11477
592	CUAUGGCA A UAGGGGCU	2729	AGCCCTCA GGCTAGCTACAACGA TGCCATAG	11478
598	CAAUGAGG G CUUAGGGU	2730	ACCCTAAG GGCTAGCTACAACGA CCTCATTG	11479
605	GGCUUAGG G UGGGCAGG	2731	CCTGCCCA GGCTAGCTACAACGA CCTAAGCC	11480
609	UAGGGUGG G CAGGAUGG	2732	CCATCCTG GGCTAGCTACAACGA CCACCCTA	11481
614	UGGGCAGG A UGGCUCCU	2733	AGGAGCCA GGCTAGCTACAACGA CCTGCCCA	11482
617	GCAGGAUG G CUUCUGUC	2734	GACAGGAG GGCTAGCTACAACGA CATCCTGC	11483
623	UGGCUCCU G UCACCCCG	2735	CGGGGTGA GGCTAGCTACAACGA AGGAGCCA	11484
626	CUCCUGUC A CCCCAGCG	2736	CCGCGGGG GGCTAGCTACAACGA GACAGGAG	11485
631	GUCACCCC G CGGCUCCC	2737	GGGAGCCG GGCTAGCTACAACGA GGGGTGAC	11486
634	ACCCCGCG G CUCCCGGC	2738	GCCGGGAG GGCTAGCTACAACGA CGCGGGGT	11487
641	GGCUCCCG G CCUAGUUG	2739	CAACTAGG GGCTAGCTACAACGA CGGGAGCC	11488
646	CCGGCCUA G UUGGGGCC	2740	GGCCCCAA GGCTAGCTACAACGA TAGGCCGG	11489
652	UAGUUGGG G CCCACGG	2741	CCGTGGGG GGCTAGCTACAACGA CCCAACTA	11490
657	GGGGCCCC A CGGACCCC	2742	GGGGTCCG GGCTAGCTACAACGA GGGGCCCC	11491
661	CCCCACGG A CCCCAGGC	2743	GCCGGGGG GGCTAGCTACAACGA CCGTGGGG	11492
668	GACCCCGG G CGUAGGUC	2744	GACCTACG GGCTAGCTACAACGA CGGGGGTC	11493
670	CCCCCGGC G UAGGUCGC	2745	GCGACCTA GGCTAGCTACAACGA GCCGGGGG	11494
674	CGGCGUAG G UCGCGUAA	2746	TTACGCGA GGCTAGCTACAACGA CTACGCCG	11495
677	CGUAGGUC G CGUAACUU	2747	AAGTTACG GGCTAGCTACAACGA GACCTACG	11496
679	UAGGUCGC G UAACUUGG	2748	CCAAGTTA GGCTAGCTACAACGA GCGACCTA	11497
682	GUCGCGUA A CUUGGGUA	2749	TACCCAAG GGCTAGCTACAACGA TACGCGAC	11498
688	UAACUUGG G UAAGGUCA	2750	TGACCTTA GGCTAGCTACAACGA CCAAGTTA	11499
693	UGGGUAAG G UCAUCGAU	2751	ATCGATGA GGCTAGCTACAACGA CTTACCCA	11500
696	GUAAGGUC A UCGAUACC	2752	GGTATCGA GGCTAGCTACAACGA GACCTTAC	11501
700	GGUCAUCG A UACCCUCA	2753	TGAGGGTA GGCTAGCTACAACGA CGATGACC	11502
702	UCAUCGAU A CCCUCACA	2754	TGTGAGGG GGCTAGCTACAACGA ATCGATGA	11503
708	AUACCCUC A CAUGCGGC	2755	GCCGCATG GGCTAGCTACAACGA GAGGGTAT	11504

710	ACCCUCAC A UGCGGCUU	2756	AAGCCGCA GGCTAGCTACAACGA GTGAGGGT	11505
712	CCUCACAU G CGGCUUCG	2757	CGAAGCCG GGCTAGCTACAACGA ATGTGAGG	11506
715	CACAUGCG G CUUCGCCG	2758	CGGCGAAG GGCTAGCTACAACGA CGCATGTG	11507
720	GCGGCUUC G CCGACCUC	2759	GAGGTCGG GGCTAGCTACAACGA GAAGCCGC	11508
724	CUUCGCCG A CCUCAUGG	2760	CCATGAGG GGCTAGCTACAACGA CGGCGAAG	11509
729	CCGACCUC A UGGGGUAC	2761	GTACCCCA GGCTAGCTACAACGA GAGGTCGG	11510
734	CUCAUGGG G UACAUUCC	2762	GGAATGTA GGCTAGCTACAACGA CCCATGAG	11511
736	CAUGGGGU A CAUUCGCG	2763	GCGGAATG GGCTAGCTACAACGA ACCCCATG	11512
738	UGGGGUAC A UUCCGCUC	2764	GAGCGGAA GGCTAGCTACAACGA GTACCCCA	11513
743	UACAUUCC G CUCGUCGG	2765	CCGACGAG GGCTAGCTACAACGA GGAATGTA	11514
747	UUCCGCUC G UCGGCGCC	2766	GGCGCCGA GGCTAGCTACAACGA GAGCGGAA	11515
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753	UCGUCGGC G CCCCCUUG	2768	CAAGGGGG GGCTAGCTACAACGA GCCGACGA	11517
766	CUUGGGAG G CACUGCCA	2769	TGGCAGTG GGCTAGCTACAACGA CTCCCAAG	11518
768	UGGGAGGC A CUGCCAGG	2770	CCTGGCAG GGCTAGCTACAACGA GCCTCCCA	11519
771	GAGGCACU G CCAGGGCC	2771	GGCCCTGG GGCTAGCTACAACGA AGTGCCCTC	11520
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783	GGGCCCUG G CGCAUGGC	2773	GCCATGCG GGCTAGCTACAACGA CAGGGCCC	11522
785	GCCCUGGC G CAUGGCGU	2774	ACGCCATG GGCTAGCTACAACGA GCCAGGGC	11523
787	CCUGGCGC A UGGGCGCC	2775	GGACGCCA GGCTAGCTACAACGA GCGCCAGG	11524
790	GGCGCAUG G CGUCCGGG	2776	CCCGACAG GGCTAGCTACAACGA CATGCGCC	11525
792	CGCAUGGC G UCCGGGUU	2777	AACCCGGA GGCTAGCTACAACGA GCCATGCG	11526
798	GCGUCCGG G UUCUGGAA	2778	TTCCAGAA GGCTAGCTACAACGA CCGGACGC	11527
808	UCUGGAAG A CGGCGUGA	2779	TCACGCCG GGCTAGCTACAACGA CTTCCAGA	11528
811	GGAAGACG G CGUGAACU	2780	AGTTCACG GGCTAGCTACAACGA CGTCTTCC	11529
813	AAGACGGC G UGAACUAA	2781	ATAGTTCA GGCTAGCTACAACGA GCCGTCTT	11530
817	CGGCGUGA A CUAUGCAA	2782	TTGCATAG GGCTAGCTACAACGA TCACGCCG	11531
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822	UGAACUAA G CAACAGGG	2784	CCCTGTTG GGCTAGCTACAACGA ATAGTTCA	11533
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836	GGGAUUCU G CCCGGUUG	2787	CAACCGGG GGCTAGCTACAACGA AGATTCCC	11536
841	UCUGCCCG G UUGCUCUU	2788	AAGAGCAA GGCTAGCTACAACGA CGGGCAGA	11537
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875	GCUCUCUC G CCCUGUCU	2793	AGACAGGG GGCTAGCTACAACGA AGCAGAGC	11542
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885	CCUGUCUG A CCAUCCCA	2795	TGGGATGG GGCTAGCTACAACGA CAGACAGG	11544
888	GUCUGACC A UCCAGGCC	2796	GGCTGGGA GGCTAGCTACAACGA GGTGAGAC	11545
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911	UAUGAGGU G UGCAACGC	2801	GCGTTGCA GGCTAGCTACAACGA ACCTCATA	11550
913	UGAGGUGU G CAACGCGU	2802	ACGCGTTG GGCTAGCTACAACGA ACACCTCA	11551
916	GGUGUGCA A CGCGUCCG	2803	CGGACGCG GGCTAGCTACAACGA TGCACACC	11552
918	UGUGCAAC G CGUCCGGG	2804	CCCGGACG GGCTAGCTACAACGA GTTGCAACA	11553
920	UGCAACGC G UCCGGGCU	2805	AGCCCGGA GGCTAGCTACAACGA GCGTTGCA	11554
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929	UCCGGGCU G UACCAUGU	2807	ACATGGTA GGCTAGCTACAACGA AGCCCGGA	11556
931	CGGGCUGU A CCAUGUCA	2808	TGACATGG GGCTAGCTACAACGA ACAGCCCG	11557
934	GCUGUACC A UGUCACGA	2809	TCGTGACA GGCTAGCTACAACGA GGTACAGC	11558
936	UGUACCAU G UCACGAAC	2810	GTTCTGTA GGCTAGCTACAACGA ATGGTACA	11559
939	ACCAUGUC A CGAACGAU	2811	ATCGTTCTG GGCTAGCTACAACGA GACATGGT	11560

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949	GAACGAUU G CUCCAACU	2814	AGTTGGAG GGCTAGCTACAACGA AATCGTTC	11563
955	UUGCUCUA A CUCAAGCA	2815	TGCTTGAG GGCTAGCTACAACGA TGGAGCAA	11564
961	CAACUCAA G CAUUGUGU	2816	ACACAATG GGCTAGCTACAACGA TTGAGTTG	11565
963	ACUCAAGC A UUGUGUAU	2817	ATACACAA GGCTAGCTACAACGA GCTTGAGT	11566
966	CAAGCAUU G UGUUAGAG	2818	CTCATACA GGCTAGCTACAACGA AATGCTTG	11567
968	AGCAUUGU G UAUGAGGC	2819	GCCTCATA GGCTAGCTACAACGA ACAATGCT	11568
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975	UGUAUGAG G CAGAGGAC	2821	GTCCTCTG GGCTAGCTACAACGA CTCATACA	11570
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984	CAGAGGAC A UGAUCAUG	2823	CATGATCA GGCTAGCTACAACGA GTCCTCTG	11572
987	AGGACAUG A UCAUGCAC	2824	GTGCATGA GGCTAGCTACAACGA CATGTCTT	11573
990	ACAUGAUC A UGCACACC	2825	GGTGTGCA GGCTAGCTACAACGA GATCATGT	11574
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1015	CGUGCCCU G CGUUCGGG	2833	CCCGAACG GGCTAGCTACAACGA AGGGCACG	11582
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1086	AUGCCAGC A UCCCCACU	2850	AGTGGGGA GGCTAGCTACAACGA GCTGGCAT	11599
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1134	UUGGGGCG G CUGCUUUC	2864	GAAAGCAG GGCTAGCTACAACGA CGCCCCAA	11613
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1154	UCUGCUAU G UACGUGGG	2869	CCCACGTA GGCTAGCTACAACGA ATAGCAGA	11618
1156	UGCUAUGU A CGUGGGGG	2870	CCCCCAGG GGCTAGCTACAACGA ACATAGCA	11619
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1359	CACAAGCC G UCGUGGAC	2921	GTCCACGA GGCTAGCTACAACGA GGCTTGTG	11670
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1384	GGGGGCCC A CUGGGGAG	2928	CTCCCCAG GGCTAGCTACAACGA GGGCCCCC	11677
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1452	UGAUGUG A UGCUACUC	2943	GAGTAGCA GGCTAGCTACAACGA CACAATCA	11692
1454	AUUGUGAU G CUACUCUU	2944	AAGAGTAG GGCTAGCTACAACGA ATCACAAT	11693
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1464	UACUCUUU G CCGGCGUU	2946	AACGCCGG GGCTAGCTACAACGA AAAGAGTA	11695
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1470	UUGCCGGC G UUGACGGG	2948	CCCGTCAA GGCTAGCTACAACGA GCCGGCAA	11697
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1480	UGACGGGG A CACCUACA	2950	TGTAGGTG GGCTAGCTACAACGA CCCCCTCA	11699
1482	ACGGGGAC A CCUACACG	2951	CGTGTAGG GGCTAGCTACAACGA GTCCCCGT	11700
1486	GGACACCU A CAGACAG	2952	CTGTCTGT GGCTAGCTACAACGA AGGTGTCC	11701
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1507	GGCGCAGG G CCACACCA	2957	TGGTGTGG GGCTAGCTACAACGA CCTGCGCC	11706
1510	GCAGGGCC A CACCACUA	2958	TAGTGGTG GGCTAGCTACAACGA GGCCCTGC	11707
1512	AGGGCCAC A CCACUAGU	2959	ACTAGTGG GGCTAGCTACAACGA GTGGCCCT	11708
1515	GCCACACC A CUAGUAGG	2960	CCTACTAG GGCTAGCTACAACGA GGTGTGGC	11709
1519	CACCACUA G UAGGGUGG	2961	CCACCCTA GGCTAGCTACAACGA TAGTGGTG	11710
1524	CUAGUAGG G UGGCAUCC	2962	GGATGCCA GGCTAGCTACAACGA CCTACTAG	11711
1527	GUAGGGUG G CAUCCUC	2963	GAGGGATG GGCTAGCTACAACGA CACCCTAC	11712
1529	AGGGUGGC A UCCUCUU	2964	AAGAGGGA GGCTAGCTACAACGA GCCACCCT	11713
1539	CCCUCUUU A CAUCUGGA	2965	TCCAGATG GGCTAGCTACAACGA AAAGAGGG	11714
1541	CUCUUUAC A UCUGGAGC	2966	GCTCCAGA GGCTAGCTACAACGA GTAAAGAG	11715
1548	CAUCUGGA G CAUCUCAG	2967	CTGAGATG GGCTAGCTACAACGA TCCAGATG	11716
1550	UCUGGAGC A UCUCAGAA	2968	TTCTGAGA GGCTAGCTACAACGA GCTCCAGA	11717
1558	AUCUCAGA A UAUCACG	2969	GCTGGATA GGCTAGCTACAACGA TCTGAGAT	11718
1560	CUCAGAAU A UCCAGCUU	2970	AAGCTGGA GGCTAGCTACAACGA ATTCTGAG	11719
1565	AAUAUCCA G CUUAUUA	2971	TTAATAAG GGCTAGCTACAACGA TGATATT	11720
1569	UCCAGCUU A UUAACACC	2972	GGTGTAA GGCTAGCTACAACGA AAGCTGGA	11721
1573	GCUUAUUA A CACCAACG	2973	CGTGGTG GGCTAGCTACAACGA TAATAAGC	11722
1575	UUUAUAAC A CCAACGGC	2974	GCCGTGG GGCTAGCTACAACGA GTTAATAA	11723
1579	UAACACCA A CGGCAGCU	2975	AGTGCCTG GGCTAGCTACAACGA TGGTGTAA	11724
1582	CACCAACG G CAGCUGGC	2976	GCCAGCTG GGCTAGCTACAACGA CGTGGTGT	11725
1585	CAACGGCA G CUGGCACA	2977	TGTGCCAG GGCTAGCTACAACGA TGCCGTGT	11726
1589	GGCAGCUG G CACAUUAA	2978	TTAATGTG GGCTAGCTACAACGA CAGCTGCC	11727
1591	CAGCUGGC A CAUUAACA	2979	TGTTAATG GGCTAGCTACAACGA GCCAGCTG	11728

1593	GCUGGCAC A UUAACAGG	2980	CCTGTTAA GGCTAGCTACAACGA GTGCCAGC	11729
1597	GCACAUUA A CAGGACUG	2981	CAGTCCTG GGCTAGCTACAACGA TAATGTGC	11730
1602	UUAACAGG A CUGCCCUG	2982	CAGGGCAG GGCTAGCTACAACGA CCTGTTAA	11731
1605	ACAGGACU G CCCUGAAC	2983	GTTCAGGG GGCTAGCTACAACGA AGTCCTGT	11732
1612	UGCCCUGA A CUGCAAUG	2984	CATTGCAG GGCTAGCTACAACGA TCAGGGCA	11733
1615	CCUGAACU G CAAUGACU	2985	AGTCATTG GGCTAGCTACAACGA AGTTCAGG	11734
1618	GAACUGCA A UGACUCCC	2986	GGGAGTCA GGCTAGCTACAACGA TGCAGTTC	11735
1621	CUGCAAUG A CUCCCUCC	2987	GGAGGGAG GGCTAGCTACAACGA CATTGCAG	11736
1632	CCCUCCAA A CCGGGUUC	2988	GAACCCGG GGCTAGCTACAACGA TTGGAGGG	11737
1637	CAAACCGG G UUCAUUGC	2989	GCAATGAA GGCTAGCTACAACGA CCGGTTTG	11738
1641	CCGGGUUC A UUGCUGCA	2990	TGCAGCAA GGCTAGCTACAACGA GAACCCGG	11739
1644	GGUUCAU G CUGCACUG	2991	CAGTGCAG GGCTAGCTACAACGA AATGAACC	11740
1647	UCAUUGCU G CACUGUUC	2992	GAACAGTG GGCTAGCTACAACGA AGCAATGA	11741
1649	AUUGCUGC A CUGUUCUA	2993	TAGAACAG GGCTAGCTACAACGA GCAGCAAT	11742
1652	GCUGCACU G UUCUAUGC	2994	GCATAGAA GGCTAGCTACAACGA AGTGCAGC	11743
1657	ACUGUUCU A UGCACACA	2995	TGTGTGCA GGCTAGCTACAACGA AGAACAGT	11744
1659	UGUUCUUA G CACACAGG	2996	CCTGTGTG GGCTAGCTACAACGA ATAGAACA	11745
1661	UUCUAUGC A CACAGGUU	2997	AACCTGTG GGCTAGCTACAACGA GCATAGAA	11746
1663	CUAUGCAC A CAGGUUCA	2998	TGAACCTG GGCTAGCTACAACGA GTGCATAG	11747
1667	GACACAG G UUCAACUC	2999	GAGTTGAA GGCTAGCTACAACGA CTGTGTGC	11748
1672	CAGGUUCA A CUCGUCCG	3000	CGGACGAG GGCTAGCTACAACGA TGAACCTG	11749
1676	UUCAACUC G UCCGGAUG	3001	CATCCGGA GGCTAGCTACAACGA GAGTTGAA	11750
1682	UCGUCCGG A UGCCACAC	3002	TGTGGGCA GGCTAGCTACAACGA CCGGACGA	11751
1684	GUCCGGAU G CCCACAGC	3003	GCTGTGGG GGCTAGCTACAACGA ATCCGGAC	11752
1688	GGAUCCCC A CAGCGCUU	3004	AAGCGCTG GGCTAGCTACAACGA GGGCATCC	11753
1691	UGCCCACA G CGCUUGGC	3005	GCCAAGCG GGCTAGCTACAACGA TGTGGGCA	11754
1693	CCCACAGC G CUUGGCCA	3006	TGGCCAAG GGCTAGCTACAACGA GCTGTGGG	11755
1698	AGCGCUUG G CCAGCUGC	3007	GCAGCTGG GGCTAGCTACAACGA CAAGCGCT	11756
1702	CUUGGCCA G CUGCCGCU	3008	AGCGGCAG GGCTAGCTACAACGA TGGCCAAG	11757
1705	GGCCAGCU G CCGCUCCA	3009	TGGAGCGG GGCTAGCTACAACGA AGCTGGCC	11758
1708	CAGCUGCC G CUCCAUUG	3010	CAATGGAG GGCTAGCTACAACGA GGCAGCTG	11759
1713	GCCGCUCC A UUGACAAG	3011	CTTGTCAA GGCTAGCTACAACGA GGAGCGGC	11760
1717	CUCCAUUG A CAAGUUCG	3012	CGAACTTG GGCTAGCTACAACGA CAATGGAG	11761
1721	AUUGACAA G UUCGCUCA	3013	TGAGCGAA GGCTAGCTACAACGA TTGTCAAT	11762
1725	ACAAGUUC G CUCAGGGG	3014	CCCTGAG GGCTAGCTACAACGA GAACTTGT	11763
1733	GCUCAGGG G UGGGUCC	3015	GGACCCCA GGCTAGCTACAACGA CCCTGAGC	11764
1738	GGGUGGG G UCCUAUCA	3016	TGATAGGA GGCTAGCTACAACGA CCCACCCC	11765
1743	GGGUUCU A UCACCUAC	3017	GTAGTGGA GGCTAGCTACAACGA AGGACCCC	11766
1746	GUCCUAUC A CCUACACC	3018	GGTGTAGG GGCTAGCTACAACGA GATAGGAC	11767
1750	UAUCACCU A CACCGAGG	3019	CCTCGGTG GGCTAGCTACAACGA AGGTGATA	11768
1752	UCACCUAC A CCGAGGGC	3020	GCCCTCGG GGCTAGCTACAACGA GTAGGTGA	11769
1759	CACCGAGG G CCACAACU	3021	AGTTGTGG GGCTAGCTACAACGA CCTCGGTG	11770
1762	CGAGGGCC A CAACUCGG	3022	CCGAGTTG GGCTAGCTACAACGA GGCCCTCG	11771
1765	GGGCCACA A CUCGGACC	3023	GGTCCGAG GGCTAGCTACAACGA TGTGGCCC	11772
1771	CAACUCGG A CCAGAGGC	3024	GCCTCTGG GGCTAGCTACAACGA CCGAGTTG	11773
1778	GACCAGAG G CCCUAUUG	3025	CAATAGGG GGCTAGCTACAACGA CTCTGGTC	11774
1783	GAGGCCCU A UUGCUGGC	3026	GCCAGCAA GGCTAGCTACAACGA AGGGCCTC	11775
1786	GCCCUAU G CUGGCACU	3027	AGTGCCAG GGCTAGCTACAACGA AATAGGGC	11776
1790	UAUUGCUG G CACUACGC	3028	GCGTAGTG GGCTAGCTACAACGA CAGCAATA	11777
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1872	GCCUGUU G UGGUGGGG	3055	CCCCACCA GGCTAGCTACAACGA AACAGGGC	11804
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1907	GCCCCCAG G UAUAACUG	3064	CAGTTATA GGCTAGCTACAACGA GTGGGGGC	11813
1909	CCCCACGU A UAACUGGG	3065	CCCAGTTA GGCTAGCTACAACGA ACGTGGGG	11814
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1924	GGGGGCGA A CGAGACGG	3068	CCGTCTCG GGCTAGCTACAACGA TCGCCCCC	11817
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1935	AGACGGAC G UGCUGCUC	3071	GAGCAGCA GGCTAGCTACAACGA GTCCGTCT	11820
1937	ACGGACGU G CUGCUCU	3072	AGGACGAG GGCTAGCTACAACGA ACGTCCGT	11821
1940	GACGUGCU G CUCCUCAA	3073	TTGAGGAG GGCTAGCTACAACGA AGCACGTC	11822
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1951	CCUCAACA A CACGCGGC	3075	GCCGCGTG GGCTAGCTACAACGA TGTGAGG	11824
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1958	AACACGCG G CCGCCGCA	3078	TGCGGCGG GGCTAGCTACAACGA CGCGTGTT	11827
1961	ACGCGGCC G CCGCAAGG	3079	CCTGCGGG GGCTAGCTACAACGA GGCCGCGT	11828
1964	CGGCCGCC G CAAGGCAA	3080	TTGCCTTG GGCTAGCTACAACGA GGCGCCG	11829
1969	GCCGCAAG G CAACUGGU	3081	ACCAGTTG GGCTAGCTACAACGA CTTGCGGC	11830
1972	GCAAGGCA A CUGGUUCG	3082	CGAACCAG GGCTAGCTACAACGA TGCTTGC	11831
1976	GGCAACUG G UUCGGCUG	3083	CAGCCGAA GGCTAGCTACAACGA CAGTTGCC	11832
1981	CUGGUUCG G CUGCACAU	3084	ATGTGCAG GGCTAGCTACAACGA CGAACCCAG	11833
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1992	GCACAUGG A UGAUUGC	3088	GCCATTCA GGCTAGCTACAACGA CCATGTGC	11837
1996	AUGGAUGA A UGGCACUG	3089	CAGTGCCA GGCTAGCTACAACGA TCATCCAT	11838
1999	GAUGAAUG G CACUGGGU	3090	ACCCAGTG GGCTAGCTACAACGA CATTCATC	11839
2001	UGAAUGGC A CUGGGUUC	3091	GAACCCAG GGCTAGCTACAACGA GCCATTCA	11840

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2010	CUGGGUUC A CCAAGACG	3093	CGTCTTGG GGCTAGCTACAACGA GAACCCAG	11842
2016	UCACCAAG A CGUGCGGG	3094	CCCCGACG GGCTAGCTACAACGA CTTGGTGA	11843
2018	ACCAAGAC G UCGGGGGG	3095	CCCCCGCA GGCTAGCTACAACGA GTCTTGGT	11844
2020	CAAGACGU G CGGGGGCC	3096	GGCCCCCG GGCTAGCTACAACGA ACGTCTTG	11845
2026	GUGCGGGG G CCCCCCGU	3097	ACGGGGGG GGCTAGCTACAACGA CCCCCGAC	11846
2033	GGCCCCCC G UGCAACAU	3098	ATGTTGCA GGCTAGCTACAACGA GGGGGGCC	11847
2035	CCCCCGU G CAACAUCG	3099	CGATGTTG GGCTAGCTACAACGA ACGGGGGG	11848
2038	CCCGUGCA A CAUCGGGG	3100	CCCCGATG GGCTAGCTACAACGA TGCACGGG	11849
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2106	CCGAGGCC A CUUACGCA	3115	TGCGTAAG GGCTAGCTACAACGA GGCCTCGG	11864
2110	GGCCACUU A CGCAAAGU	3116	ACTTTGCG GGCTAGCTACAACGA AAGTGGCC	11865
2112	CCACUUA G CAAAGUGC	3117	GCACTTTG GGCTAGCTACAACGA GTAAGTGG	11866
2117	UACGCAAA G UCGGCUUC	3118	GAACCGCA GGCTAGCTACAACGA TTTGCGTA	11867
2119	CGCAAAGU G CGGUUCGG	3119	CCGAACCG GGCTAGCTACAACGA ACTTTGCG	11868
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2171	CCAUACAG G CUUUGGCA	3133	TGCCAAAG GGCTAGCTACAACGA CTGTATGG	11882
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2188	CUACCCCU G CACUGUCA	3137	TGACAGTG GGCTAGCTACAACGA AGGGGTAG	11886
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2205	AUUUUUCC A UUUUUAAG	3141	CTTAAAGA GGCTAGCTACAACGA GGAAAAAT	11890
2214	UCUUUAAG G UUAGGAUG	3142	CATCCTAA GGCTAGCTACAACGA CTTAAAGA	11891
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2222	GUUAGGAU G UAUGUGGG	3144	CCCACATA GGCTAGCTACAACGA ATCCTAAC	11893
2224	UAGGAUGU A UGUGGGGG	3145	CCCCCACA GGCTAGCTACAACGA ACATCCTA	11894
2226	GGAUGUAU G UGGGGGGC	3146	GCCCCCCA GGCTAGCTACAACGA ATACATCC	11895
2233	UGUGGGGG G CGUGGAGC	3147	GCTCCACG GGCTAGCTACAACGA CCCCCACA	11896

2235	UGGGGGGC G UGGAGCAC	3148	GTGCTCCA GGCTAGCTACAACGA GCCCCCCA	11897
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2246	GAGCACAG G CUCACCGC	3151	GCGGTGAG GGCTAGCTACAACGA CTGTGCTC	11900
2250	ACAGGCUC A CCGCCGCA	3152	TGCGGCGG GGCTAGCTACAACGA GAGCCTGT	11901
2253	GGCUCACC G CCGCAUGC	3153	GCATGCGG GGCTAGCTACAACGA GGTGAGCC	11902
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2263	CGCAUGCA A UUGGACUC	3157	GAGTCCAA GGCTAGCTACAACGA TGCATGCG	11906
2268	GCAAUUGG A CUCGAGGA	3158	TCCTCGAG GGCTAGCTACAACGA CCAATTGC	11907
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2281	AGGAGAGC G UUGUGAUU	3160	AATCACA A GGCTAGCTACAACGA GCTCTCCT	11909
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2296	UUUGGAGG A CAGGGACA	3163	TGTCCCTG GGCTAGCTACAACGA CCTCCAAA	11912
2302	GGACAGGG A CAGAUCA	3164	CTGATCTG GGCTAGCTACAACGA CCCTGTCC	11913
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2324	AGCCCGCU G CUGUUGUC	3169	GACAACAG GGCTAGCTACAACGA AGCGGGCT	11918
2327	CCGUGUCU G UUGUCCAC	3170	GTGGACAA GGCTAGCTACAACGA AGCAGCGG	11919
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2334	UGUUGUCC A CUACAGAG	3172	CTCTGTAG GGCTAGCTACAACGA GGACAACA	11921
2337	UGUCCACU A CAGAGUGG	3173	CCACTCTG GGCTAGCTACAACGA AGTGGACA	11922
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2354	CAAAUACU G CCCUGCUC	3178	GAGCAGGG GGCTAGCTACAACGA AGTATTTG	11927
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2370	CCUUCACC A CCCUACG	3181	CGGTAGGG GGCTAGCTACAACGA GGTGAAGG	11930
2375	ACCACCCU A CCGGCUCU	3182	AGAGCCGG GGCTAGCTACAACGA AGGGTGGT	11931
2379	CCCUACCG G CUCUGUCC	3183	GGACAGAG GGCTAGCTACAACGA CGGTAGGG	11932
2384	CCGGCUCU G UCCACUGG	3184	CCAGTGGA GGCTAGCTACAACGA AGAGCCGG	11933
2388	CUCUGUCC A CUGGUUUG	3185	CAAACCAG GGCTAGCTACAACGA GGACAGAG	11934
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2418	AGAACAUC G UGGACGUG	3192	CACGTCCA GGCTAGCTACAACGA GATGTTCT	11941
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2424	UCGUGGAC G UGCAAUAC	3194	GTATTGCA GGCTAGCTACAACGA GTCCACGA	11943
2426	GUGGACGU G CAAUACCU	3195	AGGTATTG GGCTAGCTACAACGA ACGTCCAC	11944
2429	GACGUGCA A UACCGUA	3196	TACAGGTA GGCTAGCTACAACGA TGCACGTC	11945
2431	CGUGCAAU A CCUGUACG	3197	CGTACAGG GGCTAGCTACAACGA ATTGCACG	11946
2435	CAAUACCU G UACGGUGU	3198	ACACCGTA GGCTAGCTACAACGA AGGTATTG	11947
2437	AUACUGU A CCGUGUAG	3199	CTACACCG GGCTAGCTACAACGA ACAGGTAT	11948
2440	CCUGUACG G UGUAGGU	3200	ACCCTACA GGCTAGCTACAACGA CGTACAGG	11949
2442	UGUACGGU G UAGGGUCA	3201	TGACCCTA GGCTAGCTACAACGA ACCGTACA	11950
2447	GGUGUAGG G UCAGCGGU	3202	ACCGCTGA GGCTAGCTACAACGA CCTACACC	11951
2451	UAGGGUCA G CGGUUGUC	3203	GACAACCG GGCTAGCTACAACGA TGACCCTA	11952

2454	GGUCAGCG G UUGUCUCC	3204	GGAGACAA GGCTAGCTACAACGA CGCTGACC	11953
2457	CAGCGGUU G UCUCUUC	3205	GAAGGAGA GGCTAGCTACAACGA AACCGCTG	11954
2466	UCUCUUC G CAAUCAA	3206	TTTGATTG GGCTAGCTACAACGA GAAGGAGA	11955
2469	CCUUCGCA A UCAAUUGG	3207	CCATTTGA GGCTAGCTACAACGA TGCGAAGG	11956
2474	GCAAUCAA A UGGGAGUA	3208	TACTCCCA GGCTAGCTACAACGA TTGATTGC	11957
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2484	GGGAGUAU G UCCUGUUG	3211	CAACAGGA GGCTAGCTACAACGA ATACTCCC	11960
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2492	GUCCUGUU G CUUUUCCU	3213	AGGAAAAG GGCTAGCTACAACGA AACAGGAC	11962
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2518	AGACGCGC G CGUCUGUG	3218	CACAGACG GGCTAGCTACAACGA GCGCGTCT	11967
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2524	GCGGUCU G UGCUGUU	3220	AACAGGCA GGCTAGCTACAACGA AGACGCGC	11969
2526	GCGUCUGU G CCUGUUUG	3221	CAAACAGG GGCTAGCTACAACGA ACAGACGC	11970
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2541	UGUGGAUG A UGCGUUG	3225	CAACAGCA GGCTAGCTACAACGA CATCCACA	11974
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2706	UCUACGGC G UAUGGCCG	3264	CGGCCATA GGCTAGCTACAACGA GCCGTAGA	12013
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3240	CGGUAGCG G UCGAGCCC	3402	GGGCTCGA GGCTAGCTACAACGA CGCTACCG	12151
3245	GCGGUCCA G CCGUCUGU	3403	ACGACGGG GGCTAGCTACAACGA TCGACCGC	12152
3249	UCGAGCCC G UCGUCUUC	3404	GAGACCGA GGCTAGCTACAACGA GGGCTCGA	12153
3252	AGCCCUGC G UCUCUCC	3405	GGAGAAGA GGCTAGCTACAACGA GACGGGCT	12154
3262	CUUCUCCG A CAUGGAAA	3406	TTTCCATG GGCTAGCTACAACGA CGGAGAAG	12155
3264	UCUCCGAC A UGGAAAUC	3407	GATTTCCA GGCTAGCTACAACGA GTCGGAGA	12156
3270	ACAUGGAA A UCAAGAUC	3408	GATCTTGA GGCTAGCTACAACGA TTCCATGT	12157
3276	AAAUCAAG A UCAUCACC	3409	GGTGATGA GGCTAGCTACAACGA CTTGATTT	12158
3279	UCAAGAUC A UCACUGG	3410	CCAGGTGA GGCTAGCTACAACGA GATCTTGA	12159
3282	AGAUCAUC A CCUGGGGG	3411	CCCCCAGG GGCTAGCTACAACGA GATGATCT	12160
3295	GGGGGGAG A CACCGCGG	3412	CCGCGGTG GGCTAGCTACAACGA CTCCCCC	12161
3297	GGGGAGAC A CCGCGCGG	3413	CGCCGCGG GGCTAGCTACAACGA GTCTCCCC	12162
3300	GAGACACC G CGGCGUGU	3414	ACACGCCG GGCTAGCTACAACGA GGTGTCTC	12163
3303	ACACCGCG G CGUGUGGG	3415	CCCACACG GGCTAGCTACAACGA CGCGGTGT	12164
3305	ACCGCGGC G UGUGGGGA	3416	TCCCCACA GGCTAGCTACAACGA GCCGCGGT	12165
3307	CGCGCGGU G UGGGGACA	3417	TGTCCCCA GGCTAGCTACAACGA ACGCCGCG	12166
3313	GUGUGGGG A CAUCAUA	3418	TAATGATG GGCTAGCTACAACGA CCCCACAC	12167
3315	GUGGGGAC A UCAUUAUG	3419	CATAATGA GGCTAGCTACAACGA GTCCCCAC	12168
3318	GGGACAUC A UUAUGGGU	3420	ACCCATAA GGCTAGCTACAACGA GATGTCCC	12169
3321	ACAUCAUU A UGGGUCUA	3421	TAGACCCA GGCTAGCTACAACGA AATGATGT	12170
3325	CAUUAUGG G UCUACCUG	3422	CAGGTAGA GGCTAGCTACAACGA CCATAATG	12171
3329	AUGGGUCU A CCUGUCUC	3423	GAGACAGG GGCTAGCTACAACGA AGACCCAT	12172
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3339	CUGUCUCC G CCCGAAGG	3425	CCTTCGGG GGCTAGCTACAACGA GGAGACAG	12174
3357	GGAGGGAG A UACUCCUA	3426	TAGGAGTA GGCTAGCTACAACGA CTCCCTCC	12175
3359	AGGGAGAU A CUCCUAGG	3427	CCTAGGAG GGCTAGCTACAACGA ATCTCCCT	12176

3368	CUCCUAGG A CCAGCCGA	3428	TCGGCTGG GGCTAGCTACAACGA CCTAGGAG	12177
3372	UAGGACCA G CCACAGU	3429	ACTGTGCG GGCTAGCTACAACGA TGGTCCTA	12178
3376	ACCAGCCG A CAGUCUUG	3430	CAAGACTG GGCTAGCTACAACGA CGGCTGGT	12179
3379	AGCCGACA G UCUGAGG	3431	CCTCAAGA GGCTAGCTACAACGA TGTGCGCT	12180
3389	CUUGAGGG G CAGGGGUG	3432	CACCCCTG GGCTAGCTACAACGA CCCTCAAG	12181
3395	GGGAGGG G UGGCGACU	3433	AGTCGCCA GGCTAGCTACAACGA CCCTGCCC	12182
3398	CAGGGGUG G CGACUCCU	3434	AGGAGTCG GGCTAGCTACAACGA CACCCCTG	12183
3401	GGGUGGCG A CUCCUCGC	3435	GCGAGGAG GGCTAGCTACAACGA CGCCACCC	12184
3408	GACUCCUC G CGCCAUU	3436	AATGGGCG GGCTAGCTACAACGA GAGGAGTC	12185
3410	CUCCUCGC G CCCAUUAC	3437	GTAATGGG GGCTAGCTACAACGA GCGAGGAG	12186
3414	UCGCGCCC A UUACGGCC	3438	GGCCGTAA GGCTAGCTACAACGA GGGCGCGA	12187
3417	CGCCCAU A CGGCCUAC	3439	GTAGGCCG GGCTAGCTACAACGA AATGGGCG	12188
3420	CCAUUACG G CCUACUCC	3440	GGAGTAGG GGCTAGCTACAACGA CGTAATGG	12189
3424	UACGGCCU A CUCCCAAC	3441	GTTGGGAG GGCTAGCTACAACGA AGGCCGTA	12190
3431	UACUCCA A CAGACGCG	3442	CGCGTCTG GGCTAGCTACAACGA TGGGAGTA	12191
3435	CCCAACAG A CGCGGGC	3443	GCCCCGCG GGCTAGCTACAACGA CTGTTGGG	12192
3437	CAACAGAG G CGGGGCCU	3444	AGGCCCGG GGCTAGCTACAACGA GTCTGTTG	12193
3442	GACGCGGG G CCUGUUUG	3445	CAAACAGG GGCTAGCTACAACGA CCCGCGTC	12194
3446	CGGGGCCU G UUUGGCUG	3446	CAGCCAAA GGCTAGCTACAACGA AGGCCCGG	12195
3451	CCUGUUUG G CUGCAUUA	3447	TAATGCAG GGCTAGCTACAACGA CAAACAGG	12196
3454	GUUUGGCU G CAUUAUCA	3448	TGATAATG GGCTAGCTACAACGA AGCCAAAC	12197
3456	UUGGCUGC A UUAUCACC	3449	GGTGATAA GGCTAGCTACAACGA GCAGCCAA	12198
3459	GCUGCAU A UCACCAGC	3450	GCTGGTGA GGCTAGCTACAACGA AATGCAGC	12199
3462	GCAUUAUC A CCAGCCUC	3451	GAGGCTGG GGCTAGCTACAACGA GATAATGC	12200
3466	UAUCACCA G CCUCACGG	3452	CCGTGAGG GGCTAGCTACAACGA TGGTGATA	12201
3471	CCAGCCUC A CGGGCCGG	3453	CCGGCCCG GGCTAGCTACAACGA GAGGCTGG	12202
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3540	CUUUCCUA G CGACCGUC	3466	GCAGGTCG GGCTAGCTACAACGA TAGGAAAG	12215
3543	UCCUAGCG A CCUGCGUC	3467	GACGCAGG GGCTAGCTACAACGA CGCTAGGA	12216
3547	AGCGACCU G CGUCAACG	3468	CGTTGACG GGCTAGCTACAACGA AGGTCGCT	12217
3549	CGACCGUC G UCAACGGC	3469	GCCGTTGA GGCTAGCTACAACGA GCAGGTCG	12218
3553	CUGCGUCA A CGGCGUGU	3470	ACACGCCG GGCTAGCTACAACGA TGACGCAG	12219
3556	CGUCAACG G CGUGUGCU	3471	AGCACACG GGCTAGCTACAACGA CGTTGACG	12220
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3570	GCUGGACU G UCUACAC	3476	GTGGTAGA GGCTAGCTACAACGA AGTCCAGC	12225
3574	GACUGUCU A CCACGGCG	3477	CGCCGTGG GGCTAGCTACAACGA AGACAGTC	12226
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3594	GCUCAAAG A CCCUAGCC	3482	GGCTAGGG GGCTAGCTACAACGA CTTTGAGC	12231
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3618	AGGGUCCA A UCACCCAA	3486	TTGGGTGA GGCTAGCTACAACGA TGGACCCT	12235
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3637	GUACACCA A UGUAGACC	3492	GGTCTACA GGCTAGCTACAACGA TGGTGATC	12241
3639	ACACCAAU G UAGACCAG	3493	CTGGTCTA GGCTAGCTACAACGA ATTGGTGT	12242
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3654	AGGACCUC G UCGGAUGG	3496	CCATCCGA GGCTAGCTACAACGA GAGGTCCT	12245
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3695	UUGACACC A UGCACCU	3506	CAGGTGCA GGCTAGCTACAACGA GGTGTCAA	12255
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3699	CACCAUGC A CCUGCGGC	3508	GCCGCGAG GGCTAGCTACAACGA GCATGGTG	12257
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3709	CUGCGCGG G CUCGGACC	3511	GGTCCGAG GGCTAGCTACAACGA CGCCGAG	12260
3715	CGGCUCCG A CCUUUACU	3512	AGTAAAGG GGCTAGCTACAACGA CCGAGCCG	12261
3721	GGACCUUU A CUUGGUCA	3513	TGACCAAG GGCTAGCTACAACGA AAAGGTCC	12262
3726	UUUACUUG G UCACGAGA	3514	TCTCGTGA GGCTAGCTACAACGA CAAGTAAA	12263
3729	ACUUGGUC A CGAGACAC	3515	GTGTCTCG GGCTAGCTACAACGA GACCAAGT	12264
3734	GUCACGAG A CACGUGA	3516	TCAGCGTG GGCTAGCTACAACGA CTCGTGAC	12265
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3766	CCGGCGGG G UGACAGCA	3526	TGCTGTCA GGCTAGCTACAACGA CCCGCCGG	12275
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3772	GGGUGACA G CAGGGGGA	3528	TCCCCTTG GGCTAGCTACAACGA TGTCACCC	12277
3781	CAGGGGGA G CUUACUUA	3529	ATAGTAAG GGCTAGCTACAACGA TCCCCTTG	12278
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3797	UCCCCCAG G CCACUUC	3532	GAGATGGG GGCTAGCTACAACGA CTGGGGGA	12281
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3833	GGCGGUCC A CUGCUCUG	3538	CAGAGCAG GGCTAGCTACAACGA GGACCGCC	12287
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3936	CUAUGGAA A CUACCAUG	3563	CATGGTAG GGCTAGCTACAACGA TTCCATAG	12312
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4015	CCACCUAC A CGCUCCCA	3583	TGGGAGCG GGCTAGCTACAACGA GTAGGTGG	12332
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4049	ACUAAGGU A CCGCUGC	3592	GCAGCCGG GGCTAGCTACAACGA ACCTTAGT	12341
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4142	UCUAAGGC A CACGGUGU	3617	ACACCGTG GGCTAGCTACAACGA GCCTTAGA	12366
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4161	AUCCUAAC A UCAGAAU	3623	AGTTCTGA GGCTAGCTACAACGA GTTAGGAT	12372
4167	ACAUCAGA A CUGGGGUA	3624	TACCCAG GGCTAGCTACAACGA TCTGATGT	12373
4173	GAACUGGG G UAAGGACC	3625	GGTCCTTA GGCTAGCTACAACGA CCCAGTTC	12374
4179	GGGUAAGG A CCAUACC	3626	GGTGATGG GGCTAGCTACAACGA CCTTACCC	12375
4182	UAAGGACC A UCACCACG	3627	CGTGGTGA GGCTAGCTACAACGA GGTCTTCA	12376
4185	GGACCAUC A CCACGGGC	3628	GCCCCGTG GGCTAGCTACAACGA GATGGTCC	12377
4188	CCAUCACC A CGGCGGCC	3629	GGCGCCCG GGCTAGCTACAACGA GGTGATGG	12378
4192	CACCACGG G CGCCCCA	3630	TGGGGGCG GGCTAGCTACAACGA CCGTGGTG	12379
4194	CCACGGGC G CCCCCAUC	3631	GATGGGGG GGCTAGCTACAACGA GCCCCGTG	12380
4200	GCGCCCCC A UCACGUAC	3632	GTACGTGA GGCTAGCTACAACGA GGGGGCGC	12381
4203	CCCCCAUC A CGUACUCC	3633	GGAGTACG GGCTAGCTACAACGA GATGGGGG	12382
4205	CCCAUCAC G UACUCCAC	3634	GTGGAGTA GGCTAGCTACAACGA GTGATGGG	12383
4207	CAUCACGU A CUCCACCU	3635	AGGTGGAG GGCTAGCTACAACGA ACGTGATG	12384
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4216	CUCCACCU A UGGCAAGU	3637	ACTTGCCA GGCTAGCTACAACGA AGGTGGAG	12386
4219	CACCUAUG G CAAGUUC	3638	GGAACCTG GGCTAGCTACAACGA CATAGGTG	12387
4223	UAUGGCAA G UUCCUUGC	3639	GCAAGGAA GGCTAGCTACAACGA TTGCCATA	12388
4230	AGUUCUUA G CCGACGGU	3640	ACCGTCGG GGCTAGCTACAACGA AAGGAACT	12389
4234	CCUUGCCG A CGGUGGUU	3641	AACCACCG GGCTAGCTACAACGA CGGCAAGG	12390
4237	UGCCGACG G UGGUUGCU	3642	AGCAACCA GGCTAGCTACAACGA CGTCGGCA	12391
4240	CGACGGUG G UUGCUCUG	3643	CAGAGCAA GGCTAGCTACAACGA CACCGTCG	12392
4243	CGGUGGUU G CUCUGGGG	3644	CCCCAGAG GGCTAGCTACAACGA AACCACCG	12393
4252	CUCUGGGG G CGCUAUG	3645	CATAGGCG GGCTAGCTACAACGA CCCCAGAG	12394
4254	CUGGGGGC G CCUAUGAC	3646	GTCATAGG GGCTAGCTACAACGA GCCCCAG	12395
4258	GGGCGCCU A UGACAUCA	3647	TGATGTCA GGCTAGCTACAACGA AGGCGCCC	12396
4261	CGCCUAUG A CAUCAUA	3648	TTATGATG GGCTAGCTACAACGA CATAGGCG	12397
4263	CCUAUGAC A UCAUAUUG	3649	CATTATGA GGCTAGCTACAACGA GTCATAGG	12398
4266	AUGACAUC A UAAUGUGU	3650	ACACATTA GGCTAGCTACAACGA GATGTCAT	12399
4269	ACAUCAUA A UGUGUGAU	3651	ATCACACA GGCTAGCTACAACGA TATGATGT	12400

4271	AUCAUAAU G UGUGAUGA	3652	TCATCACA GGCTAGCTACAACGA ATTATGAT	12401
4273	CAUAAUGU G UGAUGAGU	3653	ACTCATCA GGCTAGCTACAACGA ACATTATG	12402
4276	AAUGUGUG A UGAGUGCC	3654	GGCACTCA GGCTAGCTACAACGA CACACATT	12403
4280	UGUGAUGA G UGCCACUC	3655	GAGTGGCA GGCTAGCTACAACGA TCATCACA	12404
4282	UGAUGAGU G CCACUCAA	3656	TTGAGTGG GGCTAGCTACAACGA ACTCATCA	12405
4285	UGAGUGCC A CUCAAUUG	3657	CAATTGAG GGCTAGCTACAACGA GGCACTCA	12406
4290	GCCACUCA A UUGACUCG	3658	CGAGTCAA GGCTAGCTACAACGA TGAGTGGC	12407
4294	CUCAAUUG A CUCGACUU	3659	AAGTCGAG GGCTAGCTACAACGA CAATTGAG	12408
4299	UUGACUCG A CUUCCAUU	3660	AATGGAAG GGCTAGCTACAACGA CGAGTCAA	12409
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4312	CAUUUUGG G CAUCGGCA	3662	TGCCGATG GGCTAGCTACAACGA CCAAATG	12411
4314	UUUUUGGC A UCGGCACA	3663	TGTGCCGA GGCTAGCTACAACGA GCCCAAAA	12412
4318	GGGCAUCG G CACAGUCC	3664	GGACTGTG GGCTAGCTACAACGA CGATGCCC	12413
4320	GCAUCGGC A CAGUCCUG	3665	CAGGACTG GGCTAGCTACAACGA GCCGATGC	12414
4323	UCGGCACA G UCCUGGAC	3666	GTCCAGGA GGCTAGCTACAACGA TGTGCCGA	12415
4330	AGUCCUGG A CCAAGCGG	3667	CCGCTTGG GGCTAGCTACAACGA CCAGGACT	12416
4335	UGGACCAA G CGGAGACG	3668	CGTCTCCG GGCTAGCTACAACGA TTGGTCCA	12417
4341	AAGCGGAG A CGGCUGGA	3669	TCCAGCCG GGCTAGCTACAACGA CTCGCTT	12418
4344	CGGAGACG G CUGGAGCG	3670	CGCTCCAG GGCTAGCTACAACGA CGTCTCCG	12419
4350	CGGCUGGA G CGCGGCUC	3671	GAGCCCGG GGCTAGCTACAACGA TCCAGCCG	12420
4352	GCUGGAGC G CGGCUCGU	3672	ACGAGCCG GGCTAGCTACAACGA GCTCCAGC	12421
4355	GGAGCGCG G CUCGUCGU	3673	ACGACGAG GGCTAGCTACAACGA CGCGCTCC	12422
4359	CGCGGCUC G UCGUGCUC	3674	GAGCACGA GGCTAGCTACAACGA GAGCCGCG	12423
4362	GGCUCGUC G UGCUCGCC	3675	GGCGAGCA GGCTAGCTACAACGA GACGAGCC	12424
4364	CUCGUCGU G CUCGCCAC	3676	GTGGCGAG GGCTAGCTACAACGA ACGACGAG	12425
4368	UCGUGCUC G CCACCGCU	3677	AGCGGTGG GGCTAGCTACAACGA GAGCACGA	12426
4371	UGCUCGCC A CCGCUACG	3678	CGTAGCGG GGCTAGCTACAACGA GGCGAGCA	12427
4374	UCGCCACC G CUACGCCU	3679	AGCGGTAG GGCTAGCTACAACGA GGTGCCGA	12428
4377	CCACCGCU A CGCCUCCG	3680	CGGAGGCG GGCTAGCTACAACGA AGCGGTGG	12429
4379	ACCGCUAC G CCUCGGG	3681	CCCGGAGG GGCTAGCTACAACGA GTAGCGGT	12430
4388	CCUCCGGG A UCGGUCAC	3682	GTGACCGA GGCTAGCTACAACGA CCCGGAGG	12431
4392	CGGGAUCG G UCACCGUG	3683	CACGGTGA GGCTAGCTACAACGA CGATCCCG	12432
4395	GAUCGGUC A CCGUGCCA	3684	TGGCACGG GGCTAGCTACAACGA GACCGATC	12433
4398	CGGUCACC G UCGACAU	3685	ATGTGGCA GGCTAGCTACAACGA GGTGACCG	12434
4400	GUCACCGU G CCACAUCC	3686	GGATGTGG GGCTAGCTACAACGA ACGGTGAC	12435
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4405	CGUGCCAC A UCCCAACA	3688	TGTTGGGA GGCTAGCTACAACGA GTGGCACG	12437
4411	ACAUCCCA A CAUCGAGG	3689	CCTCGATG GGCTAGCTACAACGA TGGGATGT	12438
4413	AUCCCAAC A UCGAGGAG	3690	CTCCTCGA GGCTAGCTACAACGA GTTGGGAT	12439
4422	UCGAGGAG A UAGCCUUG	3691	CAAGGCTA GGCTAGCTACAACGA CTCCTCGA	12440
4425	AGGAGUA G CCUUGUCC	3692	GGACAAGG GGCTAGCTACAACGA TATCTCCT	12441
4430	AUAGCCUU G UCCAACAC	3693	GTGTTGGA GGCTAGCTACAACGA AAGGCTAT	12442
4435	CUUGUCCA A CACCGGAG	3694	CTCCGGTG GGCTAGCTACAACGA TGGACAAG	12443
4437	UGUCCAAC A CCGGAGAG	3695	CTCTCCGG GGCTAGCTACAACGA GTTGACA	12444
4446	CCGGAGAG A UCCCUUUC	3696	GAAGGGGA GGCTAGCTACAACGA CTCTCCGG	12445
4456	CCCUUUCU A UGGCAAAG	3697	CTTTGCCA GGCTAGCTACAACGA AGAAGGGG	12446
4459	CUUCUAUG G CAAAGCCA	3698	TGGCTTTG GGCTAGCTACAACGA CATAGAAG	12447
4464	AUGGCAAA G CCAUCCCC	3699	GGGGATGG GGCTAGCTACAACGA TTTGCCAT	12448
4467	GCAAAGCC A UCCCAUC	3700	GATGGGGA GGCTAGCTACAACGA GGCTTTGC	12449
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4479	CCAUCGAG A CCAUCAAA	3702	TTTGATGG GGCTAGCTACAACGA CTCGATGG	12451
4482	UCGAGACC A UCAAAGGG	3703	CCCTTTGA GGCTAGCTACAACGA GGTCTCGA	12452
4496	GGGGGGAG G CAUCUCAU	3704	ATGAGATG GGCTAGCTACAACGA CTCCCCC	12453
4498	GGGGAGGC A UCUCUUCU	3705	AGATGAGA GGCTAGCTACAACGA GCCTCCCC	12454
4503	GGCAUCUC A UCUCUGC	3706	GCAGAAGA GGCTAGCTACAACGA GAGATGCC	12455
4510	CAUCUUCU G CCAUUGCA	3707	TGGAATGG GGCTAGCTACAACGA AGAAGATG	12456

4513	CUUCUGCC A UUCCAAGA	3708	TCTTGGAA GGCTAGCTACAACGA GGCAGAAG	12457
4526	AAGAAGAA A UGUGACGA	3709	TCGTCACA GGCTAGCTACAACGA TTCTTCTT	12458
4528	GAAGAAAU G UGACGAGC	3710	GCTCGTCA GGCTAGCTACAACGA ATTTCTTC	12459
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4535	UGUGACGA G CUCGUCGC	3712	GCAGCGAG GGCTAGCTACAACGA TCGTCACA	12461
4539	ACGAGCUC G CUGCAAAG	3713	CTTTGCAG GGCTAGCTACAACGA GAGCTCGT	12462
4542	AGCUCGCU G CAAAGCUG	3714	CAGCTTTG GGCTAGCTACAACGA AGCGAGCT	12463
4547	GCUGCAA G CUGUCGGG	3715	CCCACAG GGCTAGCTACAACGA TTTGCAGC	12464
4550	GCAAAGCU G UCGGGCCU	3716	AGGCCCGA GGCTAGCTACAACGA AGCTTTGC	12465
4555	GCUGUCGG G CCUCGGAC	3717	GTCCGAGG GGCTAGCTACAACGA CCGACAGC	12466
4562	GGCCUCGG A CUUAACGC	3718	GCGTTAAG GGCTAGCTACAACGA CCGAGGCC	12467
4567	CGGACUUA A CGCUGUAG	3719	CTACAGCG GGCTAGCTACAACGA TAAGTCCG	12468
4569	GACUUAAC G CUGUAGCG	3720	CGTACAG GGCTAGCTACAACGA GTTAAGTC	12469
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4579	UGUAGCGU A UUACCGGG	3724	CCCGGTAA GGCTAGCTACAACGA ACGCTACA	12473
4582	AGCGUAUU A CCGGGGUC	3725	GACCCCGG GGCTAGCTACAACGA AATACGCT	12474
4588	UUACCGGG G UCUCGACG	3726	CGTCGAGA GGCTAGCTACAACGA CCCGGTAA	12475
4594	GGGUCUCG A CGUGUCCG	3727	CGGACACG GGCTAGCTACAACGA CGAGACCC	12476
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4615	ACCGGCCA G CGGGGACG	3734	CGTCCCCG GGCTAGCTACAACGA TGGCCGGT	12483
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4623	GCGGGGAC G UCGUUGUC	3736	GACAACGA GGCTAGCTACAACGA GTCCCCGC	12485
4626	GGGACGUC G UUGUCGUG	3737	CACGACAA GGCTAGCTACAACGA GACGTCCC	12486
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4638	UCGUGGCA A CAGAGCU	3741	AGCGTCTG GGCTAGCTACAACGA TGCCACGA	12490
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4644	CAACAGAC G CUCUAAUG	3743	CATTAGAG GGCTAGCTACAACGA GTCTGTTG	12492
4650	ACGCUCUA A UGACGGGC	3744	GCCCGTCA GGCTAGCTACAACGA TAGAGCGT	12493
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4657	AAUGACGG G CUAUACCG	3746	CGGTATAG GGCTAGCTACAACGA CCGTCATT	12495
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4662	CGGGCUAU A CCGGCGAU	3748	ATCGCCGG GGCTAGCTACAACGA ATAGCCCG	12497
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4669	UACCGGCG A UUUUGACU	3750	AGTCAAAA GGCTAGCTACAACGA CGCCGGTA	12499
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4680	UUGACUCG G UGAUCGAC	3752	GTCGATCA GGCTAGCTACAACGA CGAGTCAA	12501
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4697	UGUAAUAC A UGUGUCAC	3758	GTGACACA GGCTAGCTACAACGA GTATTACA	12507
4699	UAAUACAU G UGUCACCC	3759	GGGTGACA GGCTAGCTACAACGA ATGTATTA	12508
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4704	CAUGUGUC A CCCAAACA	3761	TGTTTGGG GGCTAGCTACAACGA GACACATG	12510
4710	UCACCCAA A CAGUCGAC	3762	GTCGACTG GGCTAGCTACAACGA TTGGGTGA	12511
4713	CCCAAACA G UCGACUUC	3763	GAAGTCGA GGCTAGCTACAACGA TGTTTGGG	12512

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4729	CAGCUUGG A CCCUACCU	3766	AGGTAGGG GGCTAGCTACAACGA CCAAGCTG	12515
4734	UGGACCCU A CCUUCACC	3767	GGTGAAGG GGCTAGCTACAACGA AGGGTCCA	12516
4740	CUACCUUC A CCAUUGAG	3768	CTCAATGG GGCTAGCTACAACGA GAAGGTAG	12517
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4749	CCAUUGAG A CGACGACC	3770	GGTCGTCG GGCTAGCTACAACGA CTCAATGG	12519
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4760	ACGACCGU G CCCAAGA	3774	TCTTGGGG GGCTAGCTACAACGA ACGGTCGT	12523
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4770	CCCAAGAC G CAGUGUCC	3776	GGACACTG GGCTAGCTACAACGA GTCTTGGG	12525
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4775	GACGCAGU G UCCCGCUC	3778	GAGCGGGA GGCTAGCTACAACGA ACTGCGTC	12527
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4790	UCGCAGAG G CGAGGUAG	3781	CTACCTCG GGCTAGCTACAACGA CTCTGCGA	12530
4795	GAGGCGAG G UAGGACCG	3782	CGGTCTTA GGCTAGCTACAACGA CTCGCCTC	12531
4800	GAGGUAGG A CCGGUAGG	3783	CCTACCGG GGCTAGCTACAACGA CCTACCTC	12532
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4810	CGGUAGGG G CAGGAGAG	3785	CTCTCCTG GGCTAGCTACAACGA CCCTACCG	12534
4819	CAGGAGAG G CAUAUACA	3786	TGTATATG GGCTAGCTACAACGA CTCTCCTG	12535
4821	GGAGAGGC A UAUACAGG	3787	CCTGTATA GGCTAGCTACAACGA GCCTCTCC	12536
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4829	AUAUACAG G UUGUGAC	3790	GTCACAAA GGCTAGCTACAACGA CTGTATAT	12539
4833	ACAGGUUU G UGACUCCA	3791	TGGAGTCA GGCTAGCTACAACGA AAACCTGT	12540
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4860	CUUCGGGC A UGUUCGAC	3796	GTCGAACA GGCTAGCTACAACGA GCCCGAAG	12545
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4875	ACUCCUCG G UCCUGUGU	3799	ACACAGGA GGCTAGCTACAACGA CGAGGAGT	12548
4880	UCGGUCCU G UGUGAGUG	3800	CACTACA GGCTAGCTACAACGA AGGACCGA	12549
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4896	GCUAUGAC G CGGGAUGU	3806	ACATCCCG GGCTAGCTACAACGA GTCATAGC	12555
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4910	UGUGCUUG G UACGAGCU	3810	AGCTCGTA GGCTAGCTACAACGA CAAGCACA	12559
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4920	ACGAGCUC A CGCCCCGC	3813	GGCGGGCG GGCTAGCTACAACGA GAGCTCGT	12562
4922	GAGCUCAC G CCCGCCGA	3814	TCGGCGGG GGCTAGCTACAACGA GTGAGCTC	12563
4926	UCACGCCC G CCGAGACC	3815	GGTCTCGG GGCTAGCTACAACGA GGGCGTGA	12564
4932	CCGCCGAG A CUUCCGUU	3816	AACGGAGG GGCTAGCTACAACGA CTCGGCGG	12565
4938	AGACCUCC G UUAGGUUG	3817	CAACCTAA GGCTAGCTACAACGA GGAGGTCT	12566
4943	UCCGUUAG G UUGCGGGC	3818	GCCCGCAA GGCTAGCTACAACGA CTAACGGA	12567
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5041	AGAUGCCC A CUUCUGU	3840	ACAAGAAG GGCTAGCTACAACGA GGGCATCT	12589
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5055	UGUCCAG A CCAAGCAG	3842	CTGCTTGG GGCTAGCTACAACGA CTGGGACA	12591
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5074	AGGAGAAA A CCUCCCU	3845	AGGGGAGG GGCTAGCTACAACGA TTTCTCCT	12594
5083	CCUCCCU A CCUGGUAG	3846	CTACCAGG GGCTAGCTACAACGA AGGGGAGG	12595
5088	CCUACCUG G UAGCAUAC	3847	GTATGCTA GGCTAGCTACAACGA CAGGTAGG	12596
5091	ACCUGGUA G CAUACCAA	3848	TTGGTATG GGCTAGCTACAACGA TACCAGGT	12597
5093	CUGGUAGC A UACCAAGC	3849	GCTTGCTA GGCTAGCTACAACGA GCTACCAG	12598
5095	GGUAGCAU A CCAAGCCA	3850	TGGCTTGG GGCTAGCTACAACGA ATGCTACC	12599
5100	CAUACCAA G CCACAGUG	3851	CACTGTGG GGCTAGCTACAACGA TTGGTATG	12600
5103	ACCAAGCC A CAGUGGC	3852	GCACACTG GGCTAGCTACAACGA GGCTTGGT	12601
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5108	GCCACAGU G UGCGCCAG	3854	CTGGCGCA GGCTAGCTACAACGA ACTGTGGC	12603
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5112	CAGUGUGC G CCAGGGCU	3856	AGCCCTGG GGCTAGCTACAACGA GCACACTG	12605
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5135	CCACCCCC A UCGUGGGA	3860	TCCCACGA GGCTAGCTACAACGA GGGGGTGG	12609
5138	CCCCACUC G UGGGAUCA	3861	TGATCCCA GGCTAGCTACAACGA GATGGGGG	12610
5143	AUCGUGGG A UCAAAUGU	3862	ACATTTGA GGCTAGCTACAACGA CCCACGAT	12611
5148	GGGAUCAA A UGUGGAAG	3863	CTTCCACA GGCTAGCTACAACGA TTGATCCC	12612
5150	GAUCAAAU G UGGAAGUG	3864	CACTTCCA GGCTAGCTACAACGA ATTTGATC	12613
5156	AUGUGGAA G UGUCUCAC	3865	GTGAGACA GGCTAGCTACAACGA TTCCACAT	12614
5158	GUGGAAGU G UCUCACAC	3866	GTGTGAGA GGCTAGCTACAACGA ACTTCCAC	12615
5163	AGUGUCUC A CACGGCUA	3867	TAGCCGTG GGCTAGCTACAACGA GAGACACT	12616
5165	UGUCUCAC A CGCUAAA	3868	TTTAGCCG GGCTAGCTACAACGA GTGAGACA	12617
5168	CUCACACG G CUAAGCC	3869	GGCTTTAG GGCTAGCTACAACGA CGTGTGAG	12618
5174	CGGCUAAA G CCUACGCU	3870	AGCGTAGG GGCTAGCTACAACGA TTTAGCCG	12619
5178	UAAAGCCU A CGCUACAC	3871	GTGTAGCG GGCTAGCTACAACGA AGGCTTTA	12620
5180	AAGCCUAC G CUACACGG	3872	CCGTGTAG GGCTAGCTACAACGA GTAGGCTT	12621
5183	CCUACGCU A CACGGGCC	3873	GGCCCGTG GGCTAGCTACAACGA AGCGTAGG	12622
5185	UACGCUAC A CGGGCCAA	3874	TTGGCCCG GGCTAGCTACAACGA GTAGCGTA	12623
5189	CUACACGG G CCAACACC	3875	GGTGTGTG GGCTAGCTACAACGA CCGTGTAG	12624

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5195	GGGCCAAC A CCCUGCU	3877	AGCAGGGG GGCTAGCTACAACGA GTTGGCCC	12626
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5206	CCUGCUGU A UAGGCUAG	3880	CTAGCCTA GGCTAGCTACAACGA ACAGCAGG	12629
5210	CUGUAUAG G CUAGGAGC	3881	GCTCCTAG GGCTAGCTACAACGA CTATACAG	12630
5217	GGCUAGGA G CCGUCCAA	3882	TTGGACGG GGCTAGCTACAACGA TCCTAGCC	12631
5220	UAGGAGCC G UCCAAAUA	3883	ATTTTGA GGCTAGCTACAACGA GGCTCCTA	12632
5227	CGUCCAAA A UGAUGUCA	3884	TGACATCA GGCTAGCTACAACGA TTTGGACG	12633
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5232	AAAAUGAU G UCACCCUC	3886	GAGGGTGA GGCTAGCTACAACGA ATCATTTT	12635
5235	AUGAUGUC A CCCUCACA	3887	TGTGAGGG GGCTAGCTACAACGA GACATCAT	12636
5241	UCACCCUC A CACACCCC	3888	GGGGTGTG GGCTAGCTACAACGA GAGGGTGA	12637
5243	ACCCUCAC A CACCCCAU	3889	ATGGGGTG GGCTAGCTACAACGA GTGAGGGT	12638
5245	CCUCACAC A CCCCAUAA	3890	TTATGGGG GGCTAGCTACAACGA GTGTGAGG	12639
5250	CACACCCC A UAACCAA	3891	TTTGGTTA GGCTAGCTACAACGA GGGGTGTG	12640
5253	ACCCCAUA A CCAAUAC	3892	GTATTTGG GGCTAGCTACAACGA TATGGGGT	12641
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5260	AACCAAAU A CAUCAUGA	3894	TCATGATG GGCTAGCTACAACGA ATTTGGTT	12643
5262	CCAAAUAC A UCAUGACA	3895	TGTCATGA GGCTAGCTACAACGA GTATTTGG	12644
5265	AAUACAUC A UGACAUGC	3896	GCATGTCA GGCTAGCTACAACGA GATGTATT	12645
5268	ACAUCAUG A CAUGCAUG	3897	CATGCATG GGCTAGCTACAACGA CATGATGT	12646
5270	AUCAUGAC A UGCAUGUC	3898	GACATGCA GGCTAGCTACAACGA GTCATGAT	12647
5272	CAUGACAU G CAUGUCGG	3899	CCGACATG GGCTAGCTACAACGA ATGTCATG	12648
5274	UGACAUGC A UGUCGGCU	3900	AGCCGACA GGCTAGCTACAACGA GCATGTCA	12649
5276	ACAUGCAU G UCGGCUGA	3901	TCAGCCGA GGCTAGCTACAACGA ATGCATGT	12650
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5284	GUCGCGUG A CCUGGAGG	3903	CCTCCAGG GGCTAGCTACAACGA CAGCCGAC	12652
5292	ACCUGGAG G UCGUCACC	3904	GGTGACGA GGCTAGCTACAACGA CTCCAGGT	12653
5295	UGGAGGUC G UCACCAGC	3905	GCTGGTGA GGCTAGCTACAACGA GACCTCCA	12654
5298	AGGUCGUC A CCAGCACC	3906	GGTGCTGG GGCTAGCTACAACGA GACGACCT	12655
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5304	UCACCAGC A CCUGGGUG	3908	CACCCAGG GGCTAGCTACAACGA GCTGGTGA	12657
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5312	ACCUGGGU G CUAGUAGG	3910	CCTACTAG GGCTAGCTACAACGA ACCAGGT	12659
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5320	GCUAGUAG G UGGCGUCC	3912	GGACGCCA GGCTAGCTACAACGA CTACTAGC	12661
5323	AGUAGGUG G CGUCCUGG	3913	CCAGGACG GGCTAGCTACAACGA CACCTACT	12662
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5345	CUGACCGC G UAUUGCCU	3919	AGGCAATA GGCTAGCTACAACGA GCGGTCAG	12668
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5370	GCAGCGUG G UCAUUGUG	3927	CACAATGA GGCTAGCTACAACGA CACGTGTC	12676
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5851	UGUUGGCA G CAUAGGCC	4038	GGCTATG GGCTAGCTACAACGA TGCCAACA	12787
5853	UUGGCAGC A UAGGCCU	4039	AAGGCCTA GGCTAGCTACAACGA GCTGCCAA	12788
5857	CAGCAUAG G CCUUGGGA	4040	TCCCAAGG GGCTAGCTACAACGA CTATGCTG	12789
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5890	UCUGGCGG G CUAUGGAG	4047	CTCCATAG GGCTAGCTACAACGA CCGCCAGA	12796
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5967	AGGACCUG G UCAACUUA	4063	TAAGTTGA GGCTAGCTACAACGA CAGGTCCT	12812
5971	CCUGGUCA A CUUACUCC	4064	GGAGTAAG GGCTAGCTACAACGA TGACCAGG	12813
5975	GUCAACUU A CUCCUGC	4065	GCAGGGAG GGCTAGCTACAACGA AAGTTGAC	12814
5982	UACUCCU G CCAUCCUC	4066	GAGGATGG GGCTAGCTACAACGA AGGGAGTA	12815
5985	UCCUGGCC A UCCUCUCU	4067	AGAGAGGA GGCTAGCTACAACGA GGCAGGGA	12816
5998	CUCUCCUG G CGCCUGG	4068	CCAGGGCG GGCTAGCTACAACGA CAGGAGAG	12817
6000	CUCCUGGC G CCCUGGUC	4069	GACCAGGG GGCTAGCTACAACGA GCCAGGAG	12818
6006	GCGCCUG G UCGUCGGG	4070	CCCACGA GGCTAGCTACAACGA CAGGGCGC	12819
6009	CCCUGGUC G UCGGGUG	4071	CACCCCGA GGCTAGCTACAACGA GACCAGGG	12820
6015	UCGUCGGG G UGGUGUGC	4072	GCACACCA GGCTAGCTACAACGA CCCGACGA	12821
6018	UCGGGGUG G UGUGCGCA	4073	TGCGCACA GGCTAGCTACAACGA CACCCCGA	12822
6020	GGGUGGU G UGCGCAGC	4074	GCTGCGCA GGCTAGCTACAACGA ACCACCCC	12823
6022	GGUGGUGU G CGCAGCA	4075	TCGCTGCG GGCTAGCTACAACGA ACACCACC	12824
6024	UGGUGUGC G CAGCGAUA	4076	TATCGCTG GGCTAGCTACAACGA GCACACCA	12825
6027	UGUGCGCA G CGAUACUG	4077	CAGTATCG GGCTAGCTACAACGA TGCGCACA	12826
6030	GCGCAGCG A UACUGCGU	4078	ACGCAGTA GGCTAGCTACAACGA CGCTCGGC	12827
6032	GCAGCGAU A CUGCGUCG	4079	CGACGCAG GGCTAGCTACAACGA ATCGCTGC	12828
6035	GCGAUACU G CGUCGGCA	4080	TGCCGACG GGCTAGCTACAACGA AGTATCGC	12829
6037	GAUACUGC G UCGGCAUG	4081	CATGCCGA GGCTAGCTACAACGA GCAGTATC	12830
6041	CUGCGUCG G CAUGUGGG	4082	CCCACATG GGCTAGCTACAACGA CGACGCAG	12831
6043	GCGUCGGC A UGUGGGCC	4083	GGCCCACA GGCTAGCTACAACGA GCCGACGC	12832
6045	GUCGGAU G UGGGCCCA	4084	TGGGCCCA GGCTAGCTACAACGA ATGCCGAC	12833
6049	GCAUGUGG G CCCAGGAG	4085	CTCCTGGG GGCTAGCTACAACGA CCACATGC	12834
6061	AGGAGAGG G CGCUGUGC	4086	GCACAGCG GGCTAGCTACAACGA CCTCTCCT	12835
6063	GAGAGGGC G CUGUGCAG	4087	CTGCACAG GGCTAGCTACAACGA GCCCTCTC	12836
6066	AGGGCGCU G UGCAGUGG	4088	CCACTGCA GGCTAGCTACAACGA AGCGCCCT	12837
6068	GGCGCUGU G CAGUGGAU	4089	ATCCACTG GGCTAGCTACAACGA ACAGCGCC	12838
6071	GCUGUGCA G UGAUGAA	4090	TTTATCCA GGCTAGCTACAACGA TGCACAGC	12839
6075	UGCAGUGG A UGAUUCGG	4091	CCGATTCA GGCTAGCTACAACGA CCACTGCA	12840
6079	GUGGAUGA A UCGGCUGA	4092	TGACCCGA GGCTAGCTACAACGA TCATCCAC	12841
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6087	AUCGCGUG A UAGCGUUC	4094	GAACGCTA GGCTAGCTACAACGA CAGCCGAT	12843
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6092	CUGAUAGC G UUCGCUUC	4096	GAAGCGAA GGCTAGCTACAACGA GCTATCAG	12845
6096	UAGCGUUC G CUUCGCGG	4097	CCGCGAAG GGCTAGCTACAACGA GAACGCTA	12846
6101	UUCGCUUC G CGGGGCAA	4098	TTGCCCGG GGCTAGCTACAACGA GAAGCGAA	12847
6106	UUCGCGGG G CAACCAUG	4099	CATGGTTG GGCTAGCTACAACGA CCCGCGAA	12848

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6114	GCAACCAU G UCUCUCCC	4102	GGGGGAGA GGCTAGCTACAACGA ATGGTTGC	12851
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6125	UCCCCCAC G CACUAUGU	4104	ACATAGTG GGCTAGCTACAACGA GTGGGGGA	12853
6127	CCCCACGC A CUAUGUGC	4105	GCACATAG GGCTAGCTACAACGA GCGTGGGG	12854
6130	CACGCACU A UGUGCCUG	4106	CAGGCACA GGCTAGCTACAACGA AGTGCGTG	12855
6132	CGCACUAU G UGCCUGAG	4107	CTCAGGCA GGCTAGCTACAACGA ATAGTGCG	12856
6134	CACUAUGU G CCUGAGAG	4108	CTCTCAGG GGCTAGCTACAACGA ACATAGTG	12857
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6147	AGAGCGAC G CAGCGGCG	4111	CGCCGCTG GGCTAGCTACAACGA GTCGCTCT	12860
6150	GCGACGCA G CGGCGCGC	4112	GCGCGCCG GGCTAGCTACAACGA TGCGTCGC	12861
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6159	CGGCGCGC G UGACACAA	4116	TTGTGTGA GGCTAGCTACAACGA GCGCGCCG	12865
6162	CGGCGGUC A CACAAUUC	4117	GATTTGTG GGCTAGCTACAACGA GACGCGCG	12866
6164	CGCGUCAC A CAAAUCCU	4118	AGGATTTG GGCTAGCTACAACGA GTGACGCG	12867
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6178	CCUCUCCA G CCUCACCA	4120	TGTTGAGG GGCTAGCTACAACGA TGGAGAGG	12869
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6215	CUCCAUCA G UGGAUCAA	4128	TTGATCCA GGCTAGCTACAACGA TGATGGAG	12877
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6232	UGAGGACU G CUCCACGC	4132	GCGTGGAG GGCTAGCTACAACGA AGTCCTCA	12881
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6244	CACGCCAU G UUCCGGCU	4136	AGCCGGAA GGCTAGCTACAACGA ATGGCGTG	12885
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6290	UGCACGGU G UUGACUGA	4148	TCAGTCAA GGCTAGCTACAACGA ACCGTGCA	12897
6294	CGGUGUUG A UGACUUC	4149	GAAGTCAG GGCTAGCTACAACGA CAACACCG	12898
6298	GUUGACUG A CUUCAAGA	4150	TCTTGAAG GGCTAGCTACAACGA CAGTCAAC	12899
6306	ACUUCAAG A CCUGGCUU	4151	AAGCCAGG GGCTAGCTACAACGA CTTGAAGT	12900
6311	AAGACCUG G CUUCAGUC	4152	GACTGAAG GGCTAGCTACAACGA CAGGTCTT	12901
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6421	CUGCCCAU G CGGAGCGC	4177	GCGCTCCG GGCTAGCTACAACGA ATGGGCAG	12926
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6532	CACCACGG G CCCUGCA	4208	TGCAGGGG GGCTAGCTACAACGA CCGTGGTG	12957
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6559	GGCGCCAA A CUAUUCUA	4214	TAGAATAG GGCTAGCTACAACGA TTGGCGCC	12963
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6774	CAUUCAG G UCGGCUC	4267	GAGCCCGA GGCTAGCTACAACGA CTGGAATG	13016

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6795	AAUACCUG G UUGGGUCA	4272	TGACCCAA GGCTAGCTACAACGA CAGGTATT	13021
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6849	UCACGUCC A UGCUCACC	4287	GGTGAGCA GGCTAGCTACAACGA GGACGTGA	13036
6851	ACGUCCAU G CUCACCGA	4288	TCGGTGAG GGCTAGCTACAACGA ATGGACGT	13037
6855	CCAUGCUC A CCGACCCC	4289	GGGGTCCG GGCTAGCTACAACGA GAGCATGG	13038
6859	GCUCACCG A CCCUCCCC	4290	GGGAGGGG GGCTAGCTACAACGA CGGTGAGC	13039
6868	CCCUCCCC A CAUUCACG	4291	CTGTAATG GGCTAGCTACAACGA GGGAGGGG	13040
6870	CCUCCAC A UUACAGGA	4292	TCCTGTAA GGCTAGCTACAACGA GTGGGAGG	13041
6873	CCCACAUU A CAGGAGAG	4293	CTCTCCTG GGCTAGCTACAACGA AATGTGGG	13042
6882	CAGGAGAG A CGGCUAAG	4294	CTTAGCCG GGCTAGCTACAACGA CTCTCCTG	13043
6885	GAGAGACG G CUAAGCGU	4295	ACGCTTAG GGCTAGCTACAACGA CGTCTCTC	13044
6890	ACGGCUAA G CGUAGGCU	4296	AGCCTACG GGCTAGCTACAACGA TTAGCCGT	13045
6892	GGCUAAGC G UAGGCUUG	4297	CCAGCCTA GGCTAGCTACAACGA GCTTAGCC	13046
6896	AAGCGUAG G CUGGCCAG	4298	CTGGCCAG GGCTAGCTACAACGA CTACGCTT	13047
6900	GUAGGCUG G CAGGGGGG	4299	CCCCCTGG GGCTAGCTACAACGA CAGCCTAC	13048
6908	GCCAGGGG G UCUCCCCC	4300	GGGGGAGA GGCTAGCTACAACGA CCCCTGGC	13049
6924	CCUCCUUG G CCAGCUCC	4301	GGAGCTGG GGCTAGCTACAACGA CAAGGAGG	13050
6928	CUUGGCCA G CUCCUCAG	4302	CTGAGGAG GGCTAGCTACAACGA TGGCCAAG	13051
6936	GCUCCUCA G CUAGCCAG	4303	CTGGCTAG GGCTAGCTACAACGA TGAGGAGC	13052
6940	CUCAGCUA G CCAGCUGU	4304	ACAGCTGG GGCTAGCTACAACGA TAGCTGAG	13053
6944	GUAGCCA G CUGUCUGC	4305	GCAGACAG GGCTAGCTACAACGA TGGCTAGC	13054
6947	AGCCAGCU G UCUGCGCC	4306	GGCGCAGA GGCTAGCTACAACGA AGCTGGCT	13055
6951	AGCUGUCU G CGCCUUCU	4307	AGAAGCGG GGCTAGCTACAACGA AGACAGCT	13056
6953	CUGUCUGC G CCUUCUUC	4308	GAAGAAGG GGCTAGCTACAACGA GCAGACAG	13057
6966	CUUCGAAG G CGACAUAC	4309	GTATGTCG GGCTAGCTACAACGA CTTCGAAG	13058
6969	CGAAGGCG A CAUACAUU	4310	AATGTATG GGCTAGCTACAACGA CGCCTTCG	13059
6971	AAGGCGAC A UACAUUAC	4311	GTAATGTA GGCTAGCTACAACGA GTCGCTT	13060
6973	GGCGACAU A CAUUAACC	4312	GGGTAATG GGCTAGCTACAACGA ATGTCGCC	13061
6975	CGACAUAC A UUAACCAA	4313	TTGGGTAA GGCTAGCTACAACGA GTATGTCC	13062
6978	CAUACAUU A CCCAAUUA	4314	ATATTGGG GGCTAGCTACAACGA AATGTATG	13063
6983	AUUACCCA A UAUGACUC	4315	GAGTCATA GGCTAGCTACAACGA TGGGTAAT	13064
6985	UACCCAAU A UGACUCCC	4316	GGGAGTCA GGCTAGCTACAACGA ATTGGGTA	13065
6988	CCAAUAUG A CUCCCCAG	4317	CTGGGGAG GGCTAGCTACAACGA CATATTGG	13066
6997	CUCCCCAG A CUUGAGCC	4318	GGTCAAAG GGCTAGCTACAACGA CTGGGGAG	13067
7003	AGACUUUG A CCUCAUCG	4319	CGATGAGG GGCTAGCTACAACGA CAAAGTCT	13068
7008	UUGACCUC A UCGAGGCC	4320	GGCCTCGA GGCTAGCTACAACGA GAGGTCAA	13069
7014	UCAUCGAG G CCAACCUC	4321	GAGGTTGG GGCTAGCTACAACGA CTCGATGA	13070
7018	CGAGGCCA A CCUCUGU	4322	ACAGGAGG GGCTAGCTACAACGA TGGCCTCG	13071
7025	AACCUCCU G UGGCGGCA	4323	TGCCGCCA GGCTAGCTACAACGA AGGAGGTT	13072

7028	CUCCUGUG G CGGCAGGA	4324	TCCTGCCG GGCTAGCTACAACGA CACAGGAG	13073
7031	CUGUGGCG G CAGGAGAU	4325	ATCTCCTG GGCTAGCTACAACGA CGCCACAG	13074
7038	GGCAGGAG A UGGGCGGU	4326	ACCGCCCA GGCTAGCTACAACGA CTCTTGCC	13075
7042	GGAGAUGG G CGGUAACA	4327	TGTTACCG GGCTAGCTACAACGA CCATCTCC	13076
7045	GAUGGCG G UAACAUCA	4328	TGATGTTA GGCTAGCTACAACGA CGCCCATC	13077
7048	GGGCGGUA A CAUCACUC	4329	GAGTGATG GGCTAGCTACAACGA TACCGCCC	13078
7050	GCGGUAA A UCACUCGC	4330	GCGAGTGA GGCTAGCTACAACGA GTTACCGC	13079
7053	GUAACAUC A CUCGCGUG	4331	CACGCGAG GGCTAGCTACAACGA GATGTTAC	13080
7057	CAUCACUC G CGUGGAGU	4332	ACTCCACG GGCTAGCTACAACGA GAGTGATG	13081
7059	UCACUCGC G UGGAGUCA	4333	TGACTCCA GGCTAGCTACAACGA GCGAGTGA	13082
7064	CGCGUGGA G UCAGAGAA	4334	TTCTCTGA GGCTAGCTACAACGA TCCACGCG	13083
7072	GUCAGAGA A UAAGGUAG	4335	CTACCTTA GGCTAGCTACAACGA TCTCTGAC	13084
7077	AGAAUAAG G UAGUUACC	4336	GGTAACTA GGCTAGCTACAACGA CTTATTCT	13085
7080	AUAAGGUA G UUACCCUG	4337	CAGGGTAA GGCTAGCTACAACGA TACCTTAT	13086
7083	AGGUAGUU A CCCUGGAC	4338	GTCCAGGG GGCTAGCTACAACGA AACTACCT	13087
7090	UACCCUGG A CUCUUUUG	4339	CAAAAGAG GGCTAGCTACAACGA CCAGGGTA	13088
7099	CUCUUUUG A CCCGCUUC	4340	GAAGCGGG GGCTAGCTACAACGA CAAAAGAG	13089
7103	UUUGACCC G CUUCGAGC	4341	GCTCGAAG GGCTAGCTACAACGA GGGTCAAA	13090
7110	CGCUUCGA G CGGAGGAG	4342	CTCTCTCC GGCTAGCTACAACGA TCGAAGCG	13091
7120	GGAGGAGG A UGAGAGAG	4343	CTCTCTCA GGCTAGCTACAACGA CCTCTCTC	13092
7131	AGAGAGAG G UGUCCAUU	4344	AATGGACA GGCTAGCTACAACGA CTCTCTCT	13093
7133	AGAGAGGU G UCCAUUCC	4345	GGAATGGA GGCTAGCTACAACGA ACCTCTCT	13094
7137	AGGUGUCC A UUCGCGCG	4346	CGCCGGAA GGCTAGCTACAACGA GGACACCT	13095
7143	CCAUUCGG G CGGAGAUC	4347	GATCTCCG GGCTAGCTACAACGA CGGAATGG	13096
7149	CGGCGGAG A UCCUGCGG	4348	CCGCAGGA GGCTAGCTACAACGA CTCCGCCG	13097
7154	GAGAUCCU G CGGAAUUC	4349	GATTTCGG GGCTAGCTACAACGA AGGATCTC	13098
7160	CUGCGGAA A UCCAAGAA	4350	TTCTTGGA GGCTAGCTACAACGA TTCCGCAG	13099
7169	UCCAAGAA G UUUCUUC	4351	GAAGGAAA GGCTAGCTACAACGA TTCTTGGA	13100
7179	UUCCUUA G CGUUAACC	4352	GGGTAACG GGCTAGCTACAACGA TGAAGGAA	13101
7181	CCUUCAGC G UUACCCAU	4353	ATGGGTAA GGCTAGCTACAACGA GCTGAAGG	13102
7184	UCAGCGUU A CCCAUUUG	4354	CATATGGG GGCTAGCTACAACGA AACGCTGA	13103
7188	CGUUAACC A UAUGGGCA	4355	TGCCCCA GGCTAGCTACAACGA GGGTAACG	13104
7190	UUACCCAU A UGGGCACG	4356	CGTGCCCA GGCTAGCTACAACGA ATGGGTAA	13105
7194	CCAUUUGG G CAGCCCCG	4357	CGGGCGTG GGCTAGCTACAACGA CCATATGG	13106
7196	AUAUGGGC A CGCCCGGA	4358	TCCGGGCG GGCTAGCTACAACGA GCCCATAT	13107
7198	AUGGGCAC G CCCGGAUU	4359	AATCCGGG GGCTAGCTACAACGA GTGCCCAT	13108
7204	ACGCCCGG A UUACAACC	4360	GGTTGTAA GGCTAGCTACAACGA CCGGCGGT	13109
7207	CCCGGAUU A CAACCCUC	4361	GAGGGTTG GGCTAGCTACAACGA AATCCGGG	13110
7210	GGAUUACA A CCCUCCAC	4362	GTGGAGGG GGCTAGCTACAACGA TGTAATCC	13111
7217	AACCCUCC A CUACUAGA	4363	TCTAGTAG GGCTAGCTACAACGA GGAGGGTT	13112
7220	CCUCCACU A CUAGAGCC	4364	GGCTCTAG GGCTAGCTACAACGA AGTGGAGG	13113
7226	CUACUAGA G CCCUGGAA	4365	TTCCAGGG GGCTAGCTACAACGA TCTAGTAG	13114
7237	CUGAAAG A CCCAGACU	4366	AGTCTGGG GGCTAGCTACAACGA CTTTCCAG	13115
7243	AGACCCAG A CUACGUCC	4367	GGACGTAG GGCTAGCTACAACGA CTGGGTCT	13116
7246	CCCAGACU A CGUCCUC	4368	GAGGGACG GGCTAGCTACAACGA AGTCTGGG	13117
7248	CAGACUAC G UCCUCCG	4369	CGGAGGGA GGCTAGCTACAACGA GTAGTCTG	13118
7257	UCCUCCG G UGGUACAC	4370	GTGTACCA GGCTAGCTACAACGA CGGAGGGA	13119
7260	CUCGCGUG G UACACGGG	4371	CCCGTGTA GGCTAGCTACAACGA CACCGGAG	13120
7262	CCGUGUGU A CACGGGUG	4372	CACCCGTG GGCTAGCTACAACGA ACCACCGG	13121
7264	GGUGGUAC A CGGGUGCC	4373	GGCACCCG GGCTAGCTACAACGA GTACCACC	13122
7268	GUACACGG G UGCCCCAU	4374	AATGGGCA GGCTAGCTACAACGA CCGTGTAC	13123
7270	ACACGGGU G CCCAUUGC	4375	GCAATGGG GGCTAGCTACAACGA ACCCGTGT	13124
7274	GGGUGCCC A UUGCCACC	4376	GGTGGCAA GGCTAGCTACAACGA GGGCACCC	13125
7277	UGCCCAUU G CCACUUGC	4377	GCAGGTGG GGCTAGCTACAACGA AATGGGCA	13126
7280	CCAUUGCC A CCUGCCAA	4378	TTGGCAGG GGCTAGCTACAACGA GGCAATGG	13127
7284	UGCCACCU G CCAAGGCC	4379	GGCCTTGG GGCTAGCTACAACGA AGGTGGCA	13128

7290	CUGCCAAG G CCCUCCA	4380	TGGAGGGG GGCTAGCTACAACGA CTTGGCAG	13129
7299	CCCUCCA A UACCACCU	4381	AGGTGGTA GGCTAGCTACAACGA TGGAGGGG	13130
7301	CCUCCAAU A CCACCUC	4382	GGAGGTGG GGCTAGCTACAACGA ATTGGAGG	13131
7304	CCAAUACC A CCUCCACG	4383	CGTGGAGG GGCTAGCTACAACGA GGTATTGG	13132
7310	CCACCUC A CGGAGGAA	4384	TTCCTCCG GGCTAGCTACAACGA GGAGGTGG	13133
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7326	AGAGGACG G UUGUUCUG	4386	CAGAACAA GGCTAGCTACAACGA CGTCTCT	13135
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7335	UUGUUCUG A CAGAGUCC	4388	GGACTCTG GGCTAGCTACAACGA CAGAACAA	13137
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7344	CAGAGUCC A CCUGUCU	4390	AGACACGG GGCTAGCTACAACGA GGACTCTG	13139
7347	AGUCCACC G UGUUCUCU	4391	AGAAGACA GGCTAGCTACAACGA GGTGGACT	13140
7349	UCCACCGU G UCUUCUGC	4392	GCAGAAGA GGCTAGCTACAACGA ACGGTGGA	13141
7356	UGUCUUCU G CCUUGGCG	4393	CGCCAAGG GGCTAGCTACAACGA AGAAGACA	13142
7362	CUGCCUUG G CGGAGCUC	4394	GAGCTCCG GGCTAGCTACAACGA CAAGGCAG	13143
7367	UUGGCGGA G CUCGCCAC	4395	GTGGCGAG GGCTAGCTACAACGA TCCGCCAA	13144
7371	CGGAGCUC G CCACAAAG	4396	CTTTGTGG GGCTAGCTACAACGA GAGCTCCG	13145
7374	AGCUCGCC A CAAAGACC	4397	GGTCTTTG GGCTAGCTACAACGA GCGAGCT	13146
7380	CCACAAAG A CCUUCGGC	4398	GCCGAAGG GGCTAGCTACAACGA CTTTGTGG	13147
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7390	CUUCGGCA G CUCUGAAU	4400	ATTCTAGG GGCTAGCTACAACGA TGCCGAAG	13149
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7407	CAUCGGCC G CUGAUAGA	4404	TCTATCAG GGCTAGCTACAACGA GGCCGATG	13153
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7417	UGAUAGAG G UACGGCAA	4406	TTGCCGTA GGCTAGCTACAACGA CTCTATCA	13155
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7422	GAGGUACG G CAACCGCC	4408	GGCGGTTG GGCTAGCTACAACGA CGTACCTC	13157
7425	GUACGGCA A CCGCCCCC	4409	GGGGGCGG GGCTAGCTACAACGA TGCCGTAC	13158
7428	CGGCAACC G CCCCCCCC	4410	GGGGGGGG GGCTAGCTACAACGA GGTGCGCG	13159
7438	CCCCCCCG A CCAGCCCU	4411	AGGTCTGG GGCTAGCTACAACGA CGGGGGGG	13160
7443	CCGACGAG A CCUCCAAU	4412	ATTGAGAG GGCTAGCTACAACGA CTGGTCGG	13161
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7453	CUCCAAUG A CGGUGACG	4414	CGTCACCG GGCTAGCTACAACGA CATTGGAG	13163
7456	CAAUGACG G UGACGCAG	4415	CTGCGTCA GGCTAGCTACAACGA CGTCATTG	13164
7459	UGACGGUG A CGCAGGAU	4416	ATCCTGCG GGCTAGCTACAACGA CACCGTCA	13165
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7466	GACGCAGG A UCCGACGU	4418	ACGTGCGA GGCTAGCTACAACGA CCTGCGTC	13167
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7478	GACGUUGA G UCGUACUC	4421	GAGTACGA GGCTAGCTACAACGA TCAACGTC	13170
7481	GUUGAGUC G UACUCCUC	4422	GAGGAGTA GGCTAGCTACAACGA GACTCAAC	13171
7483	UGAGUCGU A CUCCUCUA	4423	TAGAGGAG GGCTAGCTACAACGA ACGACTCA	13172
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7493	UCCUCUAG G CCCCCCU	4425	AGGGGGGG GGCTAGCTACAACGA ATAGAGGA	13174
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7525	GGAUCCCG A UCUCAGCG	4428	CGCTGAGA GGCTAGCTACAACGA CGGGATCC	13177
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7573	UGGCGAGG A UGUCGUCU	4438	AGACGACA GGCTAGCTACAACGA CCTCGCCA	13187
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7585	CGUCUGCU G CUCGAUGU	4442	ACATCGAG GGCTAGCTACAACGA AGCAGACG	13191
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7659	CCAUCAAC G CGUUGAGC	4463	GCTCAACG GGCTAGCTACAACGA GTTGATGG	13212
7661	AUCAACGC G UUGAGCAA	4464	TTGCTCAA GGCTAGCTACAACGA GCGTTGAT	13213
7666	CGCGUUGA G CAACUCUU	4465	AAGAGTTG GGCTAGCTACAACGA TCAACGCG	13214
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7676	AACUCUUU G CUGCGUCA	4467	TGACGCGA GGCTAGCTACAACGA AAAGAGTT	13216
7679	UCUUGUCU G CGUACCA	4468	TTGTGACG GGCTAGCTACAACGA AGCAAAGA	13217
7681	UUUGUCUG G UCACCACA	4469	TGTGGTGA GGCTAGCTACAACGA GCAGCAAA	13218
7684	GCUGCGUC A CCACAACA	4470	TGTTGTGG GGCTAGCTACAACGA GACGCAGC	13219
7687	GCGUACAC A CAACAUGG	4471	CCATGTTG GGCTAGCTACAACGA GGTGACGC	13220
7690	UCACCACA A CAUGGUCU	4472	AGACCATG GGCTAGCTACAACGA TGTGGTGA	13221
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7707	ACGCUACA A CAUCUCGC	4478	GCGAGATG GGCTAGCTACAACGA TGTAGCGT	13227
7709	GCUACAAC A UCUCGCG	4479	CTGCGAGA GGCTAGCTACAACGA GTTGTAGC	13228
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7717	AUCUCGCA G CGCAAGCC	4481	GGCTTGCG GGCTAGCTACAACGA TGCGAGAT	13230
7719	CUCGCGAG G CAAGCCAG	4482	CTGGCTTG GGCTAGCTACAACGA GCTGCGAG	13231
7723	CAGCGCAA G CCAGCGGC	4483	GCCGCTGG GGCTAGCTACAACGA TTGCGCTG	13232
7727	GCAAGCCA G CGGCAGAA	4484	TTCTGCGG GGCTAGCTACAACGA TGGCTTGC	13233
7730	AGCCAGCG G CAGAAGAA	4485	TTCTTCTG GGCTAGCTACAACGA CGCTGGCT	13234
7740	AGAAGAAG G UCACCUUU	4486	AAAGGTGA GGCTAGCTACAACGA CTTCTTCT	13235
7743	AGAAGGUC A CCUUGAC	4487	GTCAAAGG GGCTAGCTACAACGA GACCTTCT	13236
7750	CACCUUUG A CAGACUGC	4488	GCAGTCTG GGCTAGCTACAACGA CAAAGGTG	13237
7754	UUUGACAG A CUGCAAGU	4489	ACTTGCGG GGCTAGCTACAACGA CTGTCAA	13238
7757	GACAGACU G CAAGUCCU	4490	AGGACTTG GGCTAGCTACAACGA AGTCTGTC	13239
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7785	ACCGGGAC G UGCUCAAG	4497	CTTGAGCA GGCTAGCTACAACGA GTCCCGGT	13246
7787	CGGGACGU G CUCAAGGA	4498	TCCTTGAG GGCTAGCTACAACGA ACGTCCCG	13247
7797	UCAAGGAG A UGAAGGCG	4499	CGCCTTCA GGCTAGCTACAACGA CTCCTTGA	13248
7803	AGAUGAAG G CGAAGGCG	4500	CGCCTTCG GGCTAGCTACAACGA CTTTCATCT	13249
7809	AGGCGAAG G CGUCCACA	4501	TGTGGACG GGCTAGCTACAACGA CTTGCGCT	13250
7811	GCGAAGGC G UCCACAGU	4502	ACTGTGGA GGCTAGCTACAACGA GCCTTCGC	13251
7815	AGGCGUCC A CAGUUAAG	4503	CTTAACCTG GGCTAGCTACAACGA GGACGCCT	13252
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7824	CAGUUAAG G CUAAACUU	4505	AAGTTTAG GGCTAGCTACAACGA CTTAAGCTG	13254
7829	AAGGCUAA A CUUCUAUC	4506	GATAGAAG GGCTAGCTACAACGA TTAGCCTT	13255
7835	AAACUUCU A UCCGUAGA	4507	TCTACGGA GGCTAGCTACAACGA AGAAGTTT	13256
7839	UUCUAUCU G UAGAGGAA	4508	TTCCTCTA GGCTAGCTACAACGA GGATAGAA	13257
7848	UAGAGGAA G CCUGCAGA	4509	TCTGCAGG GGCTAGCTACAACGA TTCCTCTA	13258
7852	GGAAGCCU G CAGACUGA	4510	TCAGTCTG GGCTAGCTACAACGA AGGCTTCC	13259
7856	GCCUGCAG A CUGACGCC	4511	GGCGTCAG GGCTAGCTACAACGA CTGCAGGC	13260
7860	GCAGACUG A CGCCCCCA	4512	TGGGGGCG GGCTAGCTACAACGA CAGTCTGC	13261
7862	AGACUGAC G CCCCCACA	4513	TGTGGGGG GGCTAGCTACAACGA GTCAGTCT	13262
7868	ACGCCCCC A CAUUCGGC	4514	GCCGAATG GGCTAGCTACAACGA GGGGGCGT	13263
7870	GCCCCCAC A UUCGGCCA	4515	TGGCCGAA GGCTAGCTACAACGA GTGGGGGC	13264
7875	CACAUUCG G CCAGGUCC	4516	GGACCTGG GGCTAGCTACAACGA CGAATGTG	13265
7880	UCGGCCAG G UCCAAAUU	4517	AATTTGGA GGCTAGCTACAACGA CTGGCCGA	13266
7886	AGGUCCAA A UUUGGUUA	4518	TAACCAAA GGCTAGCTACAACGA TTGGACCT	13267
7891	CAAAUUGG G UUAUGGGG	4519	CCCCATAA GGCTAGCTACAACGA CAAATTTG	13268
7894	AUUUGGUU A UGGGGCAA	4520	TGCCCCCA GGCTAGCTACAACGA AACCAAAT	13269
7899	GUUAUGGG G CAAAGGAC	4521	GTCCTTTG GGCTAGCTACAACGA CCCATAAC	13270
7906	GGCAAAGG A CGUCCGGA	4522	TCCGGACG GGCTAGCTACAACGA CCTTTGCC	13271
7908	CAAAGGAC G UCCGGAAC	4523	GTTCCGGA GGCTAGCTACAACGA GTCCTTTG	13272
7915	CGUCCGGA A CCUAUCCA	4524	TGGATAGG GGCTAGCTACAACGA TCCGGACG	13273
7919	CGGAACCU A UGACGCGG	4525	CCGTGGA GGCTAGCTACAACGA AGGTTCCG	13274
7924	CCUAUCCA G CGGGGCCG	4526	CGGCCCCG GGCTAGCTACAACGA TGGATAGG	13275
7929	CCAGCGGG G CCGUCAAC	4527	GTTGACGG GGCTAGCTACAACGA CCCGCTGG	13276
7932	GCGGGGCC G UCAACCAC	4528	GTGGTTGA GGCTAGCTACAACGA GGCCCCGC	13277
7936	GGCCGUCA A CCACAUCC	4529	GGATGTGG GGCTAGCTACAACGA TGACGGCC	13278
7939	CGUCAACC A CAUCCGCU	4530	AGCGGATG GGCTAGCTACAACGA GGTTGACG	13279
7941	UCAACCAC A UCCGCUCC	4531	GGAGCGGA GGCTAGCTACAACGA GTGGTTGA	13280
7945	CCACAUCC G CUCCGUGU	4532	ACACGGAG GGCTAGCTACAACGA GGATGTGG	13281
7950	UCCGCUCC G UGUGGAAG	4533	CTTCCACA GGCTAGCTACAACGA GGAGCGGA	13282
7952	CGCUCCGU G UGGAAGGA	4534	TCCTTCCA GGCTAGCTACAACGA ACGGAGCG	13283
7960	GUGGAAGG A CUUGCUGG	4535	CCAGCAAG GGCTAGCTACAACGA CCTTCCAC	13284
7964	AAGGACUU G CUGGAAGA	4536	TCTTCCAG GGCTAGCTACAACGA AAGTCCTT	13285
7972	GCUGGAAG A CACUGAGA	4537	TCTCAGTG GGCTAGCTACAACGA CTTCCAGC	13286
7974	UGGAAGAC A CUGAGACA	4538	TGTCTCAG GGCTAGCTACAACGA GTCTTCCA	13287
7980	ACACUGAG A CACCAAUU	4539	AATTGGTG GGCTAGCTACAACGA CTCAGTGT	13288
7982	ACUGAGAC A CCAAUUGA	4540	TCAATTGG GGCTAGCTACAACGA GTCTCAGT	13289
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7992	CAAUUGAU A CCACCAUC	4543	GATGGTGG GGCTAGCTACAACGA ATCAATTG	13292
7995	UGAUUACC A CCAUCAUG	4544	CATGATGG GGCTAGCTACAACGA GGTATCAA	13293
7998	AUACCACC A UCAUGGCA	4545	TGCCATGA GGCTAGCTACAACGA GGTGGTAT	13294
8001	CCACCAUC A UGGCAAAA	4546	TTTTGCCA GGCTAGCTACAACGA GATGGTGG	13295
8004	CCAUCAUG G CAAAAAU	4547	ATTTTTTG GGCTAGCTACAACGA CATGATGG	13296

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8016	AAAUGAG G UUUUCUGC	4549	GCAGAAA GGCTAGCTACAACGA CTCATTTT	13298
8023	GGUUUUCU G CGUCCAAC	4550	GTTGGACG GGCTAGCTACAACGA AGAAAACC	13299
8025	UUUUCUGC G UCCAACCA	4551	TGGTTGGA GGCTAGCTACAACGA GCAGAAA	13300
8030	UGCGUCCA A CCAGAGAA	4552	TTCTCTGG GGCTAGCTACAACGA TGGACGCA	13301
8044	GAAAGGAG G CCGCAAGC	4553	GCTTGCGG GGCTAGCTACAACGA CTCCTTTC	13302
8047	AGGAGGCC G CAAGCCAG	4554	CTGGCTTG GGCTAGCTACAACGA GGCCTCCT	13303
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8055	GCAAGCCA G CUCGCCUU	4556	AAGGCGAG GGCTAGCTACAACGA TGGCTTGC	13305
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8089	GGGGGUUC G UGUGUGCG	4563	CGCACACA GGCTAGCTACAACGA GAACCCCC	13312
8091	GGGUUCGU G UGUGCGAG	4564	CTCGCACA GGCTAGCTACAACGA ACGAACCC	13313
8093	GUUCGUGU G UGCGAGAA	4565	TTCTCGCA GGCTAGCTACAACGA ACACGAAC	13314
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8106	AGAAAAUG G CCCUUUAC	4568	GTAAGGG GGCTAGCTACAACGA CATTTTCT	13317
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8116	CCUUUACG A CGUGGUCU	4570	AGACCACG GGCTAGCTACAACGA CGTAAAGG	13319
8118	UUUACGAC G UGGUCUCC	4571	GGAGACCA GGCTAGCTACAACGA GTCGTAAA	13320
8121	ACGACGUG G UCUCACC	4572	GGTGGAGA GGCTAGCTACAACGA CACGTCGT	13321
8127	UGGUCUCC A CCCUCCU	4573	AGGAAGGG GGCTAGCTACAACGA GGAGACCA	13322
8139	UUCUCAG G CCGUGAUG	4574	CATCACGG GGCTAGCTACAACGA CTGAGGAA	13323
8142	CUCAGGCC G UGAUGGGC	4575	GCCCATCA GGCTAGCTACAACGA GGCCTGAG	13324
8145	AGGCCGUG A UGGGCUCU	4576	AGAGCCCA GGCTAGCTACAACGA CACGGCCT	13325
8149	CGUGAUGG G CUCUUCAU	4577	ATGAAGAG GGCTAGCTACAACGA CCATCACG	13326
8156	GGCUCUUC A UACGGAUU	4578	AATCCGTA GGCTAGCTACAACGA GAAGAGCC	13327
8158	CUCUUCAU A CGGAUUC	4579	GGAATCCG GGCTAGCTACAACGA ATGAAGAG	13328
8162	UCAUACGG A UUCAGUA	4580	TACTGGAA GGCTAGCTACAACGA CCGTATGA	13329
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8233	CCCUAUGG G CUUUGCAU	4594	ATGCAAAG GGCTAGCTACAACGA CCATAGGG	13343
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8240	GGCUUUGC A UAUGACAC	4596	GTGTGATA GGCTAGCTACAACGA GCAAAGCC	13345
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8247	CAUAUGAC A CCCGUGU	4599	ACAGCGGG GGCTAGCTACAACGA GTCATATG	13348
8251	UGACACCC G CUGUUUCG	4600	CGAAACAG GGCTAGCTACAACGA GGGTGTCA	13349
8254	CACCCGCU G UUUCGACU	4601	AGTCGAAA GGCTAGCTACAACGA AGCGGGTG	13350
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8265	UCGACUCA A CAGUCACC	4603	GGTACTG GGCTAGCTACAACGA TGAGTCGA	13352

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8278	CACCGAGA G UGACAUCC	4606	GGATGTCA GGCTAGCTACAACGA TCTCGGTG	13355
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8289	ACAUCCGU G UCGAGGAG	4610	CTCCTCGA GGCTAGCTACAACGA ACGGATGT	13359
8297	GUCGAGGA G UCAAUUUA	4611	TAAATTGA GGCTAGCTACAACGA TCCTCGAC	13360
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8314	CCAUGUUU G UGACUUGG	4616	CCAAGTCA GGCTAGCTACAACGA AACATTGG	13365
8317	AUGUUGUG A CUUGGCCC	4617	GGGCCAAG GGCTAGCTACAACGA CACAACAT	13366
8322	GUGACUUG G CCCCCGAA	4618	TTCGGGGG GGCTAGCTACAACGA CAAGTCAC	13367
8331	CCCCCGAA G CCAGACAG	4619	CTGTCTGG GGCTAGCTACAACGA TTCGGGGG	13368
8336	GAAGCCAG A CAGGCCAU	4620	ATGGCCTG GGCTAGCTACAACGA CTGGCTTC	13369
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8348	GCCAUUAG G UGCUCAC	4623	GTGAGCGA GGCTAGCTACAACGA CTTATGGC	13372
8351	AUAAGGUC G CUCACAGA	4624	TCTGTGAG GGCTAGCTACAACGA GACCTTAT	13373
8355	GGUCGCUC A CAGAGCGG	4625	CCGCTCTG GGCTAGCTACAACGA GAGCGACC	13374
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8413	CUGCGGUU A UCGCCGUU	4637	ACCGGCGA GGCTAGCTACAACGA AACCGCAG	13386
8416	CGGUUAUC G CCGGUGCC	4638	GGCACCGG GGCTAGCTACAACGA GATAACCG	13387
8420	UAUCGCGG G UCGCGCGC	4639	GCGCGGCA GGCTAGCTACAACGA CGGCGATA	13388
8422	UCGCGGUU G CCGCGCGA	4640	TCGCGCGG GGCTAGCTACAACGA ACCGCGCA	13389
8425	CCGGUGCC G CGCGAGCG	4641	CGCTCGCG GGCTAGCTACAACGA GGCACCGG	13390
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8434	CGCGAGCG G CGUGCUGA	4644	TCAGCAGG GGCTAGCTACAACGA CGCTCGCG	13393
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8438	AGCGGCGU G CUGACGAC	4646	GTCGTCAG GGCTAGCTACAACGA ACGCGCT	13395
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8445	UGCUGACG A CCAGCUGU	4648	ACAGCTGG GGCTAGCTACAACGA CGTCAGCA	13397
8449	GACGACCA G CUGUGGUA	4649	TACCACAG GGCTAGCTACAACGA TGGTCGTC	13398
8452	GACCAGCU G UGUAAUA	4650	TATTACCA GGCTAGCTACAACGA AGCTGGTC	13399
8455	CAGCUGUG G UAAUACCC	4651	GGGTATTA GGCTAGCTACAACGA CACAGCTG	13400
8458	CUGUGGUA A UACCCUCA	4652	TGAGGGTA GGCTAGCTACAACGA TACCACAG	13401
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8466	AUACCCUC A CAUGUUA	4654	GTAACATG GGCTAGCTACAACGA GAGGGTAT	13403
8468	ACCCUCAC A UGUUAUU	4655	AAGTAACA GGCTAGCTACAACGA GTGAGGGT	13404
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8481	ACUUGAAA G CCUCUGCG	4658	CGCAGAGG GGCTAGCTACAACGA TTTCAAGT	13407
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8499	CCUGUCGA G CUGCGAAG	4662	CTTCGCAG GGCTAGCTACAACGA TCGACAGG	13411
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8515	GCUCCAGG A CUGCACGA	4665	TCGTGCAG GGCTAGCTACAACGA CCTGGAGC	13414
8518	CCAGGACU G CACGAUGC	4666	GCATCGTG GGCTAGCTACAACGA AGTCCTGG	13415
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8523	ACUGCACG A UGCUCGUG	4668	CACGAGCA GGCTAGCTACAACGA CGTGCAGT	13417
8525	UGCACGAU G CUCGUGUG	4669	CACACGAG GGCTAGCTACAACGA ATCGTGCA	13418
8529	CGAUGCUC G UGUGUGGA	4670	TCCACACA GGCTAGCTACAACGA GAGCATCG	13419
8531	AUGCUCGU G UGUGGAGA	4671	TCTCCACA GGCTAGCTACAACGA ACGAGCAT	13420
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8539	GUGUGGAG A CGACCUGG	4673	CCAGGTCG GGCTAGCTACAACGA CTCCACAC	13422
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8547	ACGACCUG G UCGUUAUC	4675	GATAACGA GGCTAGCTACAACGA CAGGTCGT	13424
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8565	GUGAAAGU G CGGGGACC	4680	GGTCCCCG GGCTAGCTACAACGA ACTTTCAC	13429
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8676	AGUUGAUA A CAUCAUGC	4703	GCATGATG GGCTAGCTACAACGA TATCAACT	13452
8678	UGAUAAC A UCAUGCUC	4704	GAGCATGA GGCTAGCTACAACGA GTTATCAA	13453
8681	AUAACAUC A UGCUCUC	4705	GAGGAGCA GGCTAGCTACAACGA GATGTTAT	13454
8683	AACAUCAU G CUCCUCCA	4706	TGGAGGAG GGCTAGCTACAACGA ATGATGTT	13455
8692	CUCCUCCA A CGUAUCAG	4707	CTGATACG GGCTAGCTACAACGA TGGAGGAG	13456
8694	CCUCCAAC G UAUCAGUU	4708	AACTGATA GGCTAGCTACAACGA GTTGGAGG	13457
8696	UCCAACGU A UCAUUGC	4709	GCAACTGA GGCTAGCTACAACGA ACGTTGGA	13458
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8710	UGCACACG A UGCAUCUG	4714	CAGATGCA GGCTAGCTACAACGA CGTGTGCA	13463
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8714	CACGAUGC A UCUGGCAA	4716	TTGCCAGA GGCTAGCTACAACGA GCATCGTG	13465
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8731	AAGGGUGU A CUACCUC A	4720	TGAGGTAG GGCTAGCTACAACGA ACACCTTT	13469
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8754	ACCCACC A CCCCCCU	4726	AAGGGGGG GGCTAGCTACAACGA GGTGGGGT	13475
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8765	CCCCUUGC G CGGGCUGC	4728	GCAGCCCG GGCTAGCTACAACGA GCAAGGGG	13477
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8772	CGCGGGCU G CGUGGGAG	4730	CTCCACG GGCTAGCTACAACGA AGCCCGCG	13479
8774	CGGGCUGC G UGGGAGAC	4731	GTCTCCCA GGCTAGCTACAACGA GCAGCCCG	13480
8781	CGUGGGAG A CAGCUAGA	4732	TCTAGCTG GGCTAGCTACAACGA CTCCACG	13481
8784	GGGAGACA G CUAGAAGC	4733	GCTTCTAG GGCTAGCTACAACGA TGTCTCCC	13482
8791	AGCUAGAA G CACUCCAG	4734	CTGGAGTG GGCTAGCTACAACGA TTCTAGCT	13483
8793	CUAGAAGC A CUCCAGUC	4735	GACTGGAG GGCTAGCTACAACGA GCTTCTAG	13484
8799	GCACUCCA G UCAACUCC	4736	GGAGTTGA GGCTAGCTACAACGA TGGAGTGC	13485
8803	UCCAGUCA A CUCCUGGC	4737	GCCAGGAG GGCTAGCTACAACGA TGACTGGA	13486
8810	AACUCCUG G CUAGGCAA	4738	TTGCCTAG GGCTAGCTACAACGA CAGGAGTT	13487
8815	CUGGCUAG G CAACAUCA	4739	TGATGTTG GGCTAGCTACAACGA CTAGCCAG	13488
8818	GCUAGGCA A CAUCAUCA	4740	TGATGATG GGCTAGCTACAACGA TGCCTAGC	13489
8820	UAGGCAAC A UCAUCAUG	4741	CATGATGA GGCTAGCTACAACGA GTTGCTTA	13490
8823	GCAACAUC A UCAUGUUU	4742	AAACATGA GGCTAGCTACAACGA GATGTTGC	13491
8826	ACAUCAUC A UGUUUGCA	4743	TGCAACA GGCTAGCTACAACGA GATGATGT	13492
8828	AUCAUCAU G UUUGCACC	4744	GGTGCAA GGCTAGCTACAACGA ATGATGAT	13493
8832	UCAUGUUU G CACCCACU	4745	AGTGGGTG GGCTAGCTACAACGA AAACATGA	13494
8834	AUGUUUGC A CCCACUCU	4746	AGAGTGGG GGCTAGCTACAACGA GCAAACAT	13495
8838	UUGCACCC A CUCUAUGG	4747	CCATAGAG GGCTAGCTACAACGA GGGTGCAA	13496
8843	CCCACUCU A UGGGUAAG	4748	CTTACCCA GGCTAGCTACAACGA AGAGTGGG	13497
8847	CUCUAUGG G UAAGGAUG	4749	CATCCTTA GGCTAGCTACAACGA CCATAGAG	13498
8853	GGGUAAGG A UGAUUCUG	4750	CAGAATCA GGCTAGCTACAACGA CCTTACCC	13499
8856	UAAGGAUG A UUCUGAUG	4751	CATCAGAA GGCTAGCTACAACGA CATCCTTA	13500
8862	UGAUUCUG A UGACUCAC	4752	GTGAGTCA GGCTAGCTACAACGA CAGAATCA	13501
8865	UUCUGAUG A CUCACUUC	4753	GAAGTGAG GGCTAGCTACAACGA CATCAGAA	13502
8869	GAUGACUC A CUUCUUCU	4754	AGAAGAAG GGCTAGCTACAACGA GAGTCATC	13503
8880	UCUUCUCC A UCCUUCUA	4755	TAGAAGGA GGCTAGCTACAACGA GGAGAAGA	13504
8889	UCCUUCUA G CCCAGGAG	4756	CTCCTGGG GGCTAGCTACAACGA TAGAAGGA	13505
8897	GCCCAGGA G CAACUUGA	4757	TCAAGTTG GGCTAGCTACAACGA TCCTGGGC	13506
8900	CAGGAGCA A CUUGAGAA	4758	TTCTCAAG GGCTAGCTACAACGA TGCTCTG	13507
8910	UUGAGAAA G CCCUAGAC	4759	GTCTAGGG GGCTAGCTACAACGA TTTCTCAA	13508
8917	AGCCCUAG A CUGCCAGA	4760	TCGTGGCAG GGCTAGCTACAACGA CTAGGGCT	13509
8920	CCUAGACU G CCAGAUCU	4761	AGATCTGG GGCTAGCTACAACGA AGTCTAGG	13510
8925	ACUGCCAG A UCUACGGG	4762	CCCGTAGA GGCTAGCTACAACGA CTGGCAGT	13511
8929	CCAGAUCU A CGGGGCUU	4763	AAGCCCCG GGCTAGCTACAACGA AGATCTGG	13512
8934	UCUACGGG G CUUGUAC	4764	GTAACAAG GGCTAGCTACAACGA CCCGTAGA	13513
8938	CGGGGCUU G UUACUCCA	4765	TGGAGTAA GGCTAGCTACAACGA AAGCCCCG	13514
8941	GGCUUGUU A CUCCAUG	4766	CAATGGAG GGCTAGCTACAACGA AACAAAGC	13515
8946	GUUACUCC A UUGAGCCA	4767	TGGCTCAA GGCTAGCTACAACGA GGAGTAAC	13516
8951	UCCAUGA G CCACUUGA	4768	TCAAGTGG GGCTAGCTACAACGA TCAATGGA	13517
8954	AUUGAGCC A CUUGACCU	4769	AGGTCAAG GGCTAGCTACAACGA GGCTCAAT	13518
8959	GCCACUUG A CCUACCUC	4770	GAGGTAGG GGCTAGCTACAACGA CAAGTGGC	13519
8963	CUUGACCU A CCUCAGAU	4771	ATCTGAGG GGCTAGCTACAACGA AGGTCAAG	13520

8970	UACCUCAG A UCAUUCAG	4772	CTGAATGA GGCTAGCTACAACGA CTGAGGTA	13521
8973	CUCAGAUC A UUCAGCGA	4773	TCGCTGAA GGCTAGCTACAACGA GATCTGAG	13522
8978	AUCAUUA G CGACUCCA	4774	TGGAGTCG GGCTAGCTACAACGA TGAATGAT	13523
8981	AUUCAGCG A CUCCAUGG	4775	CCATGGAG GGCTAGCTACAACGA CGCTGAAT	13524
8986	GCGACUCC A UGGUCUUA	4776	TAAGACCA GGCTAGCTACAACGA GGAGTCGC	13525
8989	ACUCCAUG G UCUUAGCG	4777	CGCTAAGA GGCTAGCTACAACGA CATGGAGT	13526
8995	UGGUCUUA G CGCAUUUU	4778	AAAATGCG GGCTAGCTACAACGA TAAGACCA	13527
8997	GUCUUAGC G CAUUUUCA	4779	TGAAAATG GGCTAGCTACAACGA GCTAAGAC	13528
8999	CUUAGCGC A UUUUCACU	4780	AGTGAAAA GGCTAGCTACAACGA GCGCTAAG	13529
9005	GCAUUUUC A CUCCAUAG	4781	CTATGGAG GGCTAGCTACAACGA GAAAATGC	13530
9010	UUCACUCC A UAGUUACU	4782	AGTAACTA GGCTAGCTACAACGA GGAGTGAA	13531
9013	ACUCCAUA G UUACUCCC	4783	GGGAGTAA GGCTAGCTACAACGA TATGGAGT	13532
9016	CCAUAGUU A CUCCCCAG	4784	CTGGGGAG GGCTAGCTACAACGA AACTATGG	13533
9025	CUCCCCAG G UGAAAUCA	4785	TGATTTCA GGCTAGCTACAACGA CTGGGGAG	13534
9030	CAGGUGAA A UCAAUAGG	4786	CCTATTGA GGCTAGCTACAACGA TTCACCTG	13535
9034	UGAAAUCA A UAGGGUGG	4787	CCACCCTA GGCTAGCTACAACGA TGATTTCA	13536
9039	UCAAUAGG G UGGCAUCA	4788	TGATGCCA GGCTAGCTACAACGA CCTATTGA	13537
9042	AUAGGGUG G CAUCAUGC	4789	GCATGATG GGCTAGCTACAACGA CACCCTAT	13538
9044	AGGGUGGC A UCAUGCCU	4790	AGGCATGA GGCTAGCTACAACGA GCCACCCT	13539
9047	GUGGCAUC A UGCCUCAG	4791	CTGAGGCA GGCTAGCTACAACGA GATGCCAC	13540
9049	GGCAUCAU G CCUCAGGA	4792	TCCTGAGG GGCTAGCTACAACGA ATGATGCC	13541
9059	CUCAGGAA A CUUGGGGU	4793	ACCCCAAG GGCTAGCTACAACGA TTCCTGAG	13542
9066	AACUUGGG G UACCACCC	4794	GGGTGGTA GGCTAGCTACAACGA CCCAAGTT	13543
9068	CUUGGGGU A CCACCCUU	4795	AAGGGTGG GGCTAGCTACAACGA ACCCCAAG	13544
9071	GGGGUACC A CCCUUGCG	4796	CGCAAGGG GGCTAGCTACAACGA GGTACCCC	13545
9077	CCACCCUU G CGAACCUG	4797	CAGGTTCTG GGCTAGCTACAACGA AAGGGTGG	13546
9081	CCUUGCGA A CCUGGAGA	4798	TCTCCAGG GGCTAGCTACAACGA TCGCAAGG	13547
9089	ACCUGGAG A CAUCGGGC	4799	GCCCGATG GGCTAGCTACAACGA CTCCAGGT	13548
9091	CUGGAGAC A UCGGGCCA	4800	TGGCCCGA GGCTAGCTACAACGA GTCTCCAG	13549
9096	GACAUCCG G CCAGAAGU	4801	ACTTCTGG GGCTAGCTACAACGA CCGATGTC	13550
9103	GGCCAGAA G UGUUCGCG	4802	CGCGAACA GGCTAGCTACAACGA TTCTGGCC	13551
9105	CCAGAAGU G UUCGCGCU	4803	AGCGCGAA GGCTAGCTACAACGA ACTTCTGG	13552
9109	AAGUGUUC G CGCUAAGC	4804	GCTTAGCG GGCTAGCTACAACGA GAACACTT	13553
9111	GUGUUCGC G CUAAGCUA	4805	TAGCTTAG GGCTAGCTACAACGA GCGAACAC	13554
9116	CGCGUAA G CUACUGUC	4806	GACAGTAG GGCTAGCTACAACGA TTAGCGCG	13555
9119	GCUAAGCU A CUGUCCCA	4807	TGGGACAG GGCTAGCTACAACGA AGCTTAGC	13556
9122	AAGCUACU G UCCAGGG	4808	CCCTGGGA GGCTAGCTACAACGA AGTAGCTT	13557
9138	GGGGGAGG G CCGCCACC	4809	GGTGGCGG GGCTAGCTACAACGA CCTCCCCC	13558
9141	GGAGGGCC G CCACCUGU	4810	ACAGGTGG GGCTAGCTACAACGA GGCCCTCC	13559
9144	GGGCCGCC A CCUGUGGC	4811	GCCACAGG GGCTAGCTACAACGA GGCGGCC	13560
9148	CGCCACCU G UGGCAGGU	4812	ACCTGCCA GGCTAGCTACAACGA AGGTGGCG	13561
9151	CACCUGUG G CAGGUACC	4813	GGTACCTG GGCTAGCTACAACGA CACAGGTG	13562
9155	UGUGGCAG G UACCUCUU	4814	AAGAGGTA GGCTAGCTACAACGA CTGCCACA	13563
9157	UGGCAGGU A CCUCUUA	4815	TGAAGAGG GGCTAGCTACAACGA ACCTGCCA	13564
9166	CCUCUUA A CUGGGCAG	4816	CTGCCAG GGCTAGCTACAACGA TGAAGAGG	13565
9171	UCAACUGG G CAGUAAAG	4817	CTTACTTG GGCTAGCTACAACGA CCAGTTGA	13566
9174	ACUGGGCA G UAAAGACC	4818	GGTCTTTA GGCTAGCTACAACGA TGCCAGT	13567
9180	CAGUAAAG A CCAAACUC	4819	GAGTTTGG GGCTAGCTACAACGA CTTTACTG	13568
9185	AAGACCAA A CUCAAACU	4820	AGTTTGAG GGCTAGCTACAACGA TTGGTCTT	13569
9191	AAACUCAA A CUCACUCC	4821	GGAGTGAG GGCTAGCTACAACGA TTGAGTTT	13570
9195	UCAAACUC A CUCAAUC	4822	GATTGGAG GGCTAGCTACAACGA GAGTTTGA	13571
9201	UCACUCCA A UCCAGCU	4823	AGCTGGGA GGCTAGCTACAACGA TGGAGTGA	13572
9207	CAAUCCCA G CUGCGUCU	4824	AGCGCAG GGCTAGCTACAACGA TGGGATTG	13573
9210	UCCAGCU G CGUCUCAG	4825	CTGAGACG GGCTAGCTACAACGA AGCTGGGA	13574
9212	CCAGCUGC G UCUCAGUU	4826	AAGTGAGA GGCTAGCTACAACGA GCAGCTGG	13575
9218	GCGUCUCA G UUGGACUU	4827	AAGTCCAA GGCTAGCTACAACGA TGAGACGC	13576

9223	UCAGUUGG A CUUGUCCA	4828	TGGACAAG GGCTAGCTACAACGA CCAACTGA	13577
9227	UUGGACUU G UCCAACUG	4829	CAGTTGGA GGCTAGCTACAACGA AAGTCCAA	13578
9232	CUUGUCCA A CUGGUUCG	4830	CGAACCAG GGCTAGCTACAACGA TGGACAAG	13579
9236	UCCAACUG G UUCGUUGC	4831	GCAACGAA GGCTAGCTACAACGA CAGTTGGA	13580
9240	ACUGGUUC G UUGCUGGC	4832	GCCAGCAA GGCTAGCTACAACGA GAACCACT	13581
9243	GGUUCGUU G CUGGCUAC	4833	GTAGCCAG GGCTAGCTACAACGA AACGAACC	13582
9247	CGUUGCUG G CUACAGCG	4834	CGCTGTAG GGCTAGCTACAACGA CAGCAACG	13583
9250	UGCUGGCU A CAGCGGGG	4835	CCCCGCTG GGCTAGCTACAACGA AGCCAGCA	13584
9253	UGGCUACA G CGGGGGAG	4836	CTCCCCCG GGCTAGCTACAACGA TGTAGCCA	13585
9262	CGGGGGAG A CGUGUAUC	4837	GATACACG GGCTAGCTACAACGA CTCCCCCG	13586
9264	GGGGAGAC G UGUUAUC	4838	GTGATACA GGCTAGCTACAACGA GTCTCCCC	13587
9266	GGAGACGU G UAUACAG	4839	CTGTGATA GGCTAGCTACAACGA ACGTCTCC	13588
9268	AGACUGU A UCACAGCC	4840	GGCTGTGA GGCTAGCTACAACGA ACACGTCT	13589
9271	CGUGUAUC A CAGCCUGU	4841	ACAGGCTG GGCTAGCTACAACGA GATACACG	13590
9274	GUAUCACA G CCUGUCUC	4842	GAGACAGG GGCTAGCTACAACGA TGTGATAC	13591
9278	CACAGCCU G UCUCGUGC	4843	GCACGAGA GGCTAGCTACAACGA AGGCTGTG	13592
9283	CCUGUCUC G UGCCCGAC	4844	GTCGGGCA GGCTAGCTACAACGA GAGACAGG	13593
9285	UGUCUCGU G CCCGACCC	4845	GGGTCGGG GGCTAGCTACAACGA ACGAGACA	13594
9290	CGUGCCCG A CCCCGUG	4846	CAGCGGGG GGCTAGCTACAACGA CGGGCACC	13595
9295	CCGACCCC G CUGGUUCA	4847	TGAACGAG GGCTAGCTACAACGA GGGGTCCG	13596
9299	CCCCGUG G UUGAUGCU	4848	AGCATGAA GGCTAGCTACAACGA CAGCGGGG	13597
9303	GCUGGUUC A UGCUUUGC	4849	GCAAAGCA GGCTAGCTACAACGA GAACCAAG	13598
9305	UGGUUCAU G CUUUGCCU	4850	AGGCAAAG GGCTAGCTACAACGA ATGAACCA	13599
9310	CAUGCUUU G CCUACUCC	4851	GGAGTAGG GGCTAGCTACAACGA AAAGCATG	13600
9314	CUUUGCCU A CUCCUACU	4852	AGTAGGAG GGCTAGCTACAACGA AGGCAAAG	13601
9320	CUACUCCU A CUCUCCGU	4853	ACGGAGAG GGCTAGCTACAACGA AGGAGTAG	13602
9327	UACUCUCC G UAGGGGUA	4854	TACCCCTA GGCTAGCTACAACGA GGAGAGTA	13603
9333	CCGUAGGG G UAGGCAUC	4855	GATGCCTA GGCTAGCTACAACGA CCCTACGG	13604
9337	AGGGGUAG G CAUCUACC	4856	GGTAGATG GGCTAGCTACAACGA CTACCCCT	13605
9339	GGGUAGGC A UCUACCUG	4857	CAGGTAGA GGCTAGCTACAACGA GCCTACCC	13606
9343	AGGCAUCU A CCUGCUCC	4858	GGAGCAGG GGCTAGCTACAACGA AGATGCCT	13607
9347	AUCUACCU G CUCCCCAA	4859	TTGGGGAG GGCTAGCTACAACGA AGGTAGAT	13608
9355	GCUCCCCA A CCGAUGAA	4860	TTCATCGG GGCTAGCTACAACGA TGGGGAGC	13609
9359	CCCAACCG A UGAACAGG	4861	CCTGTTCA GGCTAGCTACAACGA CGGTTGGG	13610
9363	ACCGAUGA A CAGGGAGC	4862	GCTCCCTG GGCTAGCTACAACGA TCATCGGT	13611
9370	AACAGGGA G CUAAACAC	4863	GTGTTTAG GGCTAGCTACAACGA TCCCTGTT	13612
9375	GGAGCUAA A CAGUCCAG	4864	CTGGAGTG GGCTAGCTACAACGA TTAGCTCC	13613
9377	AGCUAAAC A CUCCAGGC	4865	GCCTGGAG GGCTAGCTACAACGA GTTTAGCT	13614
9384	CACUCCAG G CCAAUAGG	4866	CCTATTGG GGCTAGCTACAACGA CTGGAGTG	13615
9388	CCAGGCCA A UAGGCCAU	4867	ATGGCCTA GGCTAGCTACAACGA TGGCCTGG	13616
9392	GCCAAUAG G CCAUCCCG	4868	CGGGATGG GGCTAGCTACAACGA CTATTGGC	13617
9395	AAUAGGCC A UCCGUUUU	4869	AAACGGGA GGCTAGCTACAACGA GGCCTATT	13618
9400	GCCAUCCC G UUUUUUUU	4870	AAAAAAA GGCTAGCTACAACGA GGGATGGC	13619

Input Sequence = HPC1S1. Cut Site = R/Y

Arm Length = 8. Core Sequence = GGCTAGCTACAACGA

HPC1S1 Hepatitis C virus (strain HCV-1b, clone HCV-K1-S1), complete genome; acc#
gi|1030702|dbj|D50483.1; 9410 nt

Table XIX: HCV minus strand DNzyme and Substrate Sequence

Pos	Substrate	SeqID	DNzyme	SeqID
9413	AAAAAAA A CGGGAUGG	4871	CCATCCCG GGCTAGCTACAACGA TTTT TTTT	13620
9408	AAAACGGG A UGGCCUUAU	4872	ATAGGCCA GGCTAGCTACAACGA CCCGTTT	13621
9405	ACGGGAUG G CCUAUUGG	4873	CCAATAGG GGCTAGCTACAACGA CATCCCGT	13622
9401	GAUGGCCU A UUGCCUG	4874	CAGGCCAA GGCTAGCTACAACGA AGGCCATC	13623
9397	GCCUAUUG G CCUGGAGU	4875	ACTCCAGG GGCTAGCTACAACGA CAATAGGC	13624
9390	GGCCUGGA G UGUUAGC	4876	GCTAAACA GGCTAGCTACAACGA TCCAGGCC	13625
9388	CCUGGAGU G UUUAGCUC	4877	GAGCTAAA GGCTAGCTACAACGA ACTCCAGG	13626
9383	AGUGUUUA G CUCCUGU	4878	ACAGGGAG GGCTAGCTACAACGA TAAACACT	13627
9376	AGCUCCCU G UUCAUCGG	4879	CCGATGAA GGCTAGCTACAACGA AGGGAGCT	13628
9372	CCCUGUUC A UCGGUUGG	4880	CCAACCGA GGCTAGCTACAACGA GAACAGGG	13629
9368	GUUCAUCG G UUGGGAG	4881	CTCCCCAA GGCTAGCTACAACGA CGATGAAC	13630
9360	GUUGGGGA G CAGGUAGA	4882	TCTACCTG GGCTAGCTACAACGA TCCCCAAC	13631
9356	GGGAGCAG G UAGAUGCC	4883	GGCATCTA GGCTAGCTACAACGA CTGCTCCC	13632
9352	GCAGGUAG A UGCUUACC	4884	GGTAGGCA GGCTAGCTACAACGA CTACCTGC	13633
9350	AGGUAGAU G CCUACCCC	4885	GGGGTAGG GGCTAGCTACAACGA ATCTACCT	13634
9346	AGAUGCCU A CCCCUACG	4886	CGTAGGGG GGCTAGCTACAACGA AGGCATCT	13635
9340	CUACCCCU A CGGAGAGU	4887	ACTCTCCG GGCTAGCTACAACGA AGGGGTAG	13636
9333	UACGGAGA G UAGGAGUA	4888	TACTCCTA GGCTAGCTACAACGA TCTCCGTA	13637
9327	GAGUAGGA G UAGGCAAA	4889	TTTGCCCTA GGCTAGCTACAACGA TCCTACTC	13638
9323	AGGAGUAG G CAAAGCAU	4890	ATGCTTTG GGCTAGCTACAACGA CTACTCCT	13639
9318	UAGGCAAA G CAUGAACC	4891	GGTTCATG GGCTAGCTACAACGA TTTGCCTA	13640
9316	GGCAAAGC A UGAACCAG	4892	CTGGTTCA GGCTAGCTACAACGA GCTTTGCC	13641
9312	AAGCAUGA A CCAGCGGG	4893	CCCGCTGG GGCTAGCTACAACGA TCATGCTT	13642
9308	AUGAACCA G CGGGGUCG	4894	CGACCCCG GGCTAGCTACAACGA TGGTTCAT	13643
9303	CCAGCGGG G UCGGGCAC	4895	GTGCCCGA GGCTAGCTACAACGA CCCGCTGG	13644
9298	GGGGUCGG G CAGGAGAC	4896	GTCTCGTG GGCTAGCTACAACGA CCGACCCC	13645
9296	GGUCGGGC A CGAGACAG	4897	CTGTCTCG GGCTAGCTACAACGA GCCCGACC	13646
9291	GGCACGAG A CAGGCUGU	4898	ACAGCCTG GGCTAGCTACAACGA CTCGTGCC	13647
9287	CGAGACAG G CUGUGAUA	4899	TATCACAG GGCTAGCTACAACGA CTGTCTCG	13648
9284	GACAGGCU G UGAUACAC	4900	GTGTATCA GGCTAGCTACAACGA AGCCTGTC	13649
9281	AGGCUGUG A UACACGUC	4901	GACGTGTA GGCTAGCTACAACGA CACAGCCT	13650
9279	GCUGUGAU A CACGUCUC	4902	GAGACGTG GGCTAGCTACAACGA ATCACAGC	13651
9277	UGUGAUAC A CGUCUCCC	4903	GGGAGACG GGCTAGCTACAACGA GTATCACA	13652
9275	UGAUACAC G UCUCUCCC	4904	GGGGGAGA GGCTAGCTACAACGA GTGTATCA	13653
9266	UCUCUCCC G CUGUAGCC	4905	GGCTACAG GGCTAGCTACAACGA GGGGGAGA	13654
9263	CCCCCGCU G UAGCCAGC	4906	GCTGGCTA GGCTAGCTACAACGA AGCGGGGG	13655
9260	CCGCUGUA G CCAGCAAC	4907	GTTGCTGG GGCTAGCTACAACGA TACAGCGG	13656
9256	UGUAGCCA G CAACGAAC	4908	GTTCTGTG GGCTAGCTACAACGA TGGCTACA	13657
9253	AGCCAGCA A CGAACCAG	4909	CTGGTTCTG GGCTAGCTACAACGA TGCTGGCT	13658
9249	AGCAACGA A CCAGUUGG	4910	CCAACCTGG GGCTAGCTACAACGA TCGTTGCT	13659
9245	ACGAACCA G UUGGACAA	4911	TTGTCCAA GGCTAGCTACAACGA TGGTTCGT	13660
9240	CCAGUUGG A CAAGUCCA	4912	TGGACTTG GGCTAGCTACAACGA CCAACTGG	13661
9236	UUGGACAA G UCCAACUG	4913	CAGTTTGA GGCTAGCTACAACGA TTGTCCAA	13662
9231	CAAGUCCA A CUGAGACG	4914	CGTCTCAG GGCTAGCTACAACGA TGGACTTG	13663
9225	CAACUGAG A CGCAGCUG	4915	CAGCTGCG GGCTAGCTACAACGA CTCAGTTG	13664
9223	ACUGAGAC G CAGCUGGG	4916	CCCAGCTG GGCTAGCTACAACGA GTCTCAGT	13665
9220	GAGACGCA G CUGGGAUU	4917	AATCCCAG GGCTAGCTACAACGA TGCGTCTC	13666
9214	CAGCUGGG A UUGGAGUG	4918	CACTCCAA GGCTAGCTACAACGA CCCAGCTG	13667
9208	GGAUUGGA G UGAGUUUG	4919	CAAACCTCA GGCTAGCTACAACGA TCCAATCC	13668
9204	UGGAGUGA G UUGAGUUU	4920	AACTCAA GGCTAGCTACAACGA TCACTCCA	13669
9198	GAGUUUGA G UUGGUCU	4921	AGACCAAA GGCTAGCTACAACGA TCAAACCT	13670

9193	UGAGUUUG G UCUUUACU	4922	AGTAAAGA GGCTAGCTACAACGA CAAACTCA	13671
9187	UGGUCUUU A CUGCCCAG	4923	CTGGGCAG GGCTAGCTACAACGA AAAGACCA	13672
9184	UCUUUACU G CCCAGUUG	4924	CAACTGGG GGCTAGCTACAACGA AGTAAAGA	13673
9179	ACUGCCCA G UUGAAGAG	4925	CTCTTCAA GGCTAGCTACAACGA TGGGCAGT	13674
9170	UUGAAGAG G UACCUGCC	4926	GGCAGGTA GGCTAGCTACAACGA CTCTTCAA	13675
9168	GAAGAGGU A CCUGCCAC	4927	GTGGCAGG GGCTAGCTACAACGA ACCTCTTC	13676
9164	AGGUACCU G CCACAGGU	4928	ACCTGTGG GGCTAGCTACAACGA AGGTACCT	13677
9161	UACCUGCC A CAGGUGGC	4929	GCCACCTG GGCTAGCTACAACGA GGCAGGTA	13678
9157	UGCCACAG G UGGCGGCC	4930	GGCCGCCA GGCTAGCTACAACGA CTGTGGCA	13679
9154	CACAGGUG G CGGCCUC	4931	GAGGGCCG GGCTAGCTACAACGA CACCTGTG	13680
9151	AGGUGGCG G CCCUCCCC	4932	GGGGAGGG GGCTAGCTACAACGA CGCCACCT	13681
9135	CCCCUGGG A CAGUAGCU	4933	AGCTACTG GGCTAGCTACAACGA CCCAGGGG	13682
9132	CUGGGACA G UAGCUUAG	4934	CTAAGCTA GGCTAGCTACAACGA TGTCCCAG	13683
9129	GGACAGUA G CUUAGCGC	4935	GCGCTAAG GGCTAGCTACAACGA TACTGTCC	13684
9124	GUAGCUUA G CGCGAACA	4936	TGTTGCGG GGCTAGCTACAACGA TAAGTAC	13685
9122	AGCUUAGC G CGAACACU	4937	AGTGTTCG GGCTAGCTACAACGA GCTAAGCT	13686
9118	UAGCGCGA A CACUUCUG	4938	CAGAAGTG GGCTAGCTACAACGA TCGCGCTA	13687
9116	GCGCGAAC A CUUCUGGC	4939	GCCAGAAG GGCTAGCTACAACGA GTTCGCGC	13688
9109	CACUUCUG G CCCGAUGU	4940	ACATCGGG GGCTAGCTACAACGA CAGAAGTG	13689
9104	CUGGCCCG A UGUCCCA	4941	TGGAGACA GGCTAGCTACAACGA CGGGCCAG	13690
9102	GGCCCGAU G UCUCAGG	4942	CCTGGAGA GGCTAGCTACAACGA ATCGGGCC	13691
9094	GUCUCCAG G UUCGCAAG	4943	CTTGCGAA GGCTAGCTACAACGA CTGGAGAC	13692
9090	CCAGGUUC G CAAGGGUG	4944	CACCTTGG GGCTAGCTACAACGA GAACCTGG	13693
9084	UCGCAAGG G UGGUACCC	4945	GGGTACCA GGCTAGCTACAACGA CCTTGCGA	13694
9081	CAAGGGUG G UACCCCAA	4946	TTGGGGTA GGCTAGCTACAACGA CACCTTGG	13695
9079	AGGGUGGU A CCCCAAGU	4947	ACTTGGGG GGCTAGCTACAACGA ACCACCTT	13696
9072	UACCCCAA G UUUCUGA	4948	TCAGGAAA GGCTAGCTACAACGA TTGGGGTA	13697
9062	UUCCUGAG G CAUGAUGC	4949	GCATCATG GGCTAGCTACAACGA CTCAGGAA	13698
9060	CCUGAGGC A UGAUGCCA	4950	TGGCATCA GGCTAGCTACAACGA GCCTCAGG	13699
9057	GAGGCAUG A UGCCACCC	4951	GGGTGGCA GGCTAGCTACAACGA CATGCCTC	13700
9055	GGCAUGAU G CCACCUA	4952	TAGGGTGG GGCTAGCTACAACGA ATCATGCC	13701
9052	AUGAUGCC A CCCUAUUG	4953	CAATAGGG GGCTAGCTACAACGA GGCATCAT	13702
9047	GCCACCCU A UUGAUUUC	4954	GAAATCAA GGCTAGCTACAACGA AGGGTGGC	13703
9043	CCCUAUUG A UUUCACCU	4955	AGGTGAAA GGCTAGCTACAACGA CAATAGGG	13704
9038	UUGAUUUC A CCUGGGGA	4956	TCCCCAGG GGCTAGCTACAACGA GAAATCAA	13705
9029	CCUGGGGA G UAACUAUG	4957	CATAGTTA GGCTAGCTACAACGA TCCCCAGG	13706
9026	GGGGAGUA A CUAUGGAG	4958	CTCCATAG GGCTAGCTACAACGA TACTCCCC	13707
9023	GAGUAACU A UGGAGUGA	4959	TCACTCCA GGCTAGCTACAACGA AGTTACTC	13708
9018	ACUAUGGA G UGAAAUG	4960	CATTTTCA GGCTAGCTACAACGA TCCATAGT	13709
9012	GAGUGAAA A UGCGCUAA	4961	TTAGCGCA GGCTAGCTACAACGA TTTCACTC	13710
9010	GUGAAAAU G CGCUAAGA	4962	TCTTAGCG GGCTAGCTACAACGA ATTTTCAC	13711
9008	GAAAAUGC G CUAAGACC	4963	GGTCTTAG GGCTAGCTACAACGA GCATTTTC	13712
9002	GCGCUAAG A CCAUGGAG	4964	CTCCATGG GGCTAGCTACAACGA CTTAGCGC	13713
8999	CUAAGACC A UGGAGUCG	4965	CGACTCCA GGCTAGCTACAACGA GGTCTTAG	13714
8994	ACCAUGGA G UCGUGAA	4966	TTCAGCGA GGCTAGCTACAACGA TCCATGGT	13715
8991	AUGGAGUC G CUGAAUGA	4967	TCATTTCG GGCTAGCTACAACGA GACTCCAT	13716
8986	GUCGCUGA A UGAUCUGA	4968	TCAGATCA GGCTAGCTACAACGA TCAGCGAC	13717
8983	GCUGAAUG A UCUGAGGU	4969	ACCTCAGA GGCTAGCTACAACGA CATTGAGC	13718
8976	GAUCUGAG G UAGGUCAA	4970	TTGACCTA GGCTAGCTACAACGA CTCAGATC	13719
8972	UGAGGUAG G UCAAGUGG	4971	CCACTTGA GGCTAGCTACAACGA CTACTTCA	13720
8967	UAGGUCAA G UGGCUCAA	4972	TTGAGCCA GGCTAGCTACAACGA TTGACCTA	13721
8964	GUCAAGUG G CUCAAUGG	4973	CCATTGAG GGCTAGCTACAACGA CACTTGAC	13722
8959	GUGGCUCA A UGGAGUAA	4974	TTACTCCA GGCTAGCTACAACGA TGAGCCAC	13723
8954	UCAAUGGA G UAACAAGC	4975	GCTTGTTA GGCTAGCTACAACGA TCCATTGA	13724
8951	AUGGAGUA A CAAGCCCC	4976	GGGGCTTG GGCTAGCTACAACGA TACTCCAT	13725
8947	AGUAACAA G CCCCUGAG	4977	CTACGGGG GGCTAGCTACAACGA TTGTTACT	13726

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8933	UAGAUCUG G CAGUCUAG	4980	CTAGACTG GGCTAGCTACAACGA CAGATCTA	13729
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8923	AGUCUAGG G CUUUCUCA	4982	TGAGAAAG GGCTAGCTACAACGA CCTAGACT	13731
8913	UUUCUCAA G UUGCUCU	4983	AGGAGCAA GGCTAGCTACAACGA TTGAGAAA	13732
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8893	CUAGAAGG A UGGAGAAG	4986	CTTCTCCA GGCTAGCTACAACGA CCTTCTAG	13735
8882	GAGAAGAA G UGAGUCAU	4987	ATGACTCA GGCTAGCTACAACGA TTCTTCTC	13736
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8875	AGUGAGUC A UCAGAAUC	4989	GATTCTGA GGCTAGCTACAACGA GACTCACT	13738
8869	UCAUCAGA A UCAUCCU	4990	AAGGATGA GGCTAGCTACAACGA TCTGATGA	13739
8866	UCAGAAUC A UCCUUAAC	4991	GGTAAGGA GGCTAGCTACAACGA GATTCTGA	13740
8860	UCAUCCU A CCCAUAGA	4992	TCTATGGG GGCTAGCTACAACGA AAGGATGA	13741
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8851	CCCAUAGA G UGGUGCA	4994	TGCACCCA GGCTAGCTACAACGA TCTATGGG	13743
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8839	GUGCAAAC A UGAUGAUG	4998	CATCATCA GGCTAGCTACAACGA GTTTCAC	13747
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8833	ACAUGAUG A UGUUGCCU	5000	AGGCAACA GGCTAGCTACAACGA CATCATGT	13749
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8804	ACUGGAGU G CUUCUAGC	5007	GCTAGAAG GGCTAGCTACAACGA ACTCCAGT	13756
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8794	UUCUAGCU G UCUCAC	5009	GTGGGAGA GGCTAGCTACAACGA AGCTAGAA	13758
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8251	UGUCAUUAU G CAAAGCCC	5146	GGGCTTTG GGCTAGCTACAACGA ATATGACA	13895
8246	UAUGCAAA G CCCAUAGG	5147	CCTATGGG GGCTAGCTACAACGA TTTGCATA	13896
8242	CAAAGCCC A UAGGGCAU	5148	ATGCCCTA GGCTAGCTACAACGA GGGCTTTG	13897
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8235	CAUAGGGC A UUUCUUUG	5150	CAAAGAAA GGCTAGCTACAACGA GCCCTATG	13899
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8152	CCAUCACG G CCUGAGGA	5167	TCCTCAGG GGCTAGCTACAACGA CGTGATGG	13916
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8129	GAGACCAC G UCGUAAAG	5171	CTTTACGA GGCTAGCTACAACGA GTGGTCTC	13920
8126	ACCACGUC G UAAAGGGC	5172	GCCCTTTA GGCTAGCTACAACGA GACGTGGT	13921
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8116	AAAGGGCC .A UUUCUCG	5174	CGAGAAA GGCTAGCTACAACGA GGCCCTTT	13923
8108	AUUUUCUC G CACACACG	5175	CGTGTGTG GGCTAGCTACAACGA GAGAAAAT	13924
8106	UUUCUCGC A CACACGAA	5176	TTCGTGTG GGCTAGCTACAACGA GCGAGAAA	13925
8104	UCUCGCAC A CACGAACC	5177	GGTTCGTG GGCTAGCTACAACGA GTGCGAGA	13926
8102	UCGCACAC A CGAACCCC	5178	GGGGTTTC GGCTAGCTACAACGA GTGTGCGA	13927
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8090	ACCCCCAA G UCUGGGAA	5180	TTCCCGAG GGCTAGCTACAACGA TTGGGGGT	13929
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8080	CUGGGAAC A CGAUAAAG	5182	CCTTATCG GGCTAGCTACAACGA GTTCCCAG	13931
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8072	ACGAUAAG G CGAGCUGG	5184	CCAGCTCG GGCTAGCTACAACGA CTTATCGT	13933
8068	UAAGGCGA G CUGGCUUG	5185	CAAGCCAG GGCTAGCTACAACGA TCGCCTTA	13934
8064	GCGAGCUG G CUUGCGGC	5186	GCCGCAAG GGCTAGCTACAACGA CAGCTCGC	13935
8060	GCUGGCUU G CGGCCUCC	5187	GGAGGCCG GGCTAGCTACAACGA AAGCCAGC	13936
8057	GGCUGCG G CCUCCUUU	5188	AAAGGAGG GGCTAGCTACAACGA CGCAAGCC	13937
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8038	CUGGUUGG A CGCAGAAA	5190	TTTCTGCG GGCTAGCTACAACGA CCAACCAG	13939
8036	GGUUGGAC G CAGAAAAC	5191	GTTTTCTG GGCTAGCTACAACGA GTCCAACC	13940
8029	CGCAGAAA A CCUCAUUU	5192	AAATGAGG GGCTAGCTACAACGA TTTCTGCG	13941
8024	AAAACCUC A UUUUUUGC	5193	GCAAAAA GGCTAGCTACAACGA GAGTTTTT	13942
8017	CAUUUUUU G CCAUGAUG	5194	CATCATGG GGCTAGCTACAACGA AAAAAATG	13943
8014	UUUUUGCC A UGAUGGUG	5195	CACCATCA GGCTAGCTACAACGA GGCAAAAA	13944
8011	UUGCAUG A UGGUGGUA	5196	TACCACCA GGCTAGCTACAACGA CATGGCAA	13945
8008	CCAUGAUG G UGGUAUCA	5197	TGATACCA GGCTAGCTACAACGA CATCATGG	13946
8005	UGAUGGUG G UAUCAAUU	5198	AATTGATA GGCTAGCTACAACGA CACCATCA	13947
8003	AUGGUGGU A UCAAUUGG	5199	CCAATTGA GGCTAGCTACAACGA ACCACCAT	13948
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7995	AUCAAUUG G UGUCUCAG	5201	CTGAGACA GGCTAGCTACAACGA CAATTGAT	13950

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7985	GUCUCAGU G UCUCACAG	5204	CTGGAAGA GGCTAGCTACAACGA ACTGAGAC	13953
7977	GUCUCCA G CAAGUCCU	5205	AGGACTTG GGCTAGCTACAACGA TGGAGAC	13954
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7963	CCUCCAC A CGGAGCGG	5208	CCGCTCCG GGCTAGCTACAACGA GTGGAAGG	13957
7958	CACACGA G CGGAUGUG	5209	CACATCCG GGCTAGCTACAACGA TCCGTGTG	13958
7954	CGGAGCGG A UGUGGUUG	5210	CAACCACA GGCTAGCTACAACGA CCGCTCCG	13959
7952	GAGCGGAU G UGUUGAC	5211	GTCAACCA GGCTAGCTACAACGA ATCCGCTC	13960
7949	CGGAUGUG G UUGACGGC	5212	GCCGTCAA GGCTAGCTACAACGA CACATCCG	13961
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7928	CUGGAUAG G UCCCGGAC	5217	GTCCGGAA GGCTAGCTACAACGA CTATCCAG	13966
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7919	UUCCGGAC G UCCUUGC	5219	GCAAAGGA GGCTAGCTACAACGA GTCCGGAA	13968
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7881	GGCCGAU G UGGGGCG	5227	CGCCCCA GGCTAGCTACAACGA ATTCGGCC	13976
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7837	GAAGUUUA G CCUUAACU	5236	AGTTAAGG GGCTAGCTACAACGA TAAACTTC	13985
7831	UAGCCUUA A CUGUGGAC	5237	GTCCACAG GGCTAGCTACAACGA TAAGGCTA	13986
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7824	AACUGUGG A CGCCUUCG	5239	CGAAGGCG GGCTAGCTACAACGA CCACAGTT	13988
7822	CUGUGGAC G CCUUCGCC	5240	GGCGAAGG GGCTAGCTACAACGA GTCCACAG	13989
7816	ACGCCUUC G CCUUCAUC	5241	GATGAAGG GGCTAGCTACAACGA GAAGGCGT	13990
7810	UCGCCUUC A UCUCUUG	5242	CAAGGAGA GGCTAGCTACAACGA GAAGGCGA	13991
7800	CUCCUUGA G CAGUCCC	5243	GGGACGTG GGCTAGCTACAACGA TCAAGGAG	13992
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7796	UUGAGCAC G UCCCGGUA	5245	TACCGGGA GGCTAGCTACAACGA GTGCTCAA	13994
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7770	CAGGACUU G CAGUCUGU	5251	ACAGACTG GGCTAGCTACAACGA AAGTCTGT	14000
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7743	CUUCUUCU G CCGCUGGC	5256	GCCAGCGG GGCTAGCTACAACGA AGAAGAAG	14005
7740	CUUCUGCC G CUGGCUUG	5257	CAAGCCAG GGCTAGCTACAACGA GGCAGAAG	14006

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7730	UGGCUUGC G CUGCGAGA	5260	TCTCGCAG GGCTAGCTACAACGA GCAAGCCA	14009
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7722	GCUGCGAG A UGUUGUAG	5262	CTACAACA GGCTAGCTACAACGA CTCGCAGC	14011
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7694	UUGUGGUG A CGCAGCAA	5272	TTGTGTCG GGCTAGCTACAACGA CACCACAA	14021
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7679	AAAGAGUU G CUCAACGC	5276	GCGTTGAG GGCTAGCTACAACGA AACTCTTT	14025
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7256	GGGACGUA G UCUGGGUC	5374	GACCCAGA GGCTAGCTACAACGA TACGTCCC	14123
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7173	CUUCUUGG A UUUCGCA	5391	TGCGGAAA GGCTAGCTACAACGA CCAAGAAG	14140
7167	GGAUUUCC G CAGGAUCU	5392	AGATCCTG GGCTAGCTACAACGA GGAAATCC	14141
7162	UCCGCAGG A UCUCGCC	5393	GGCGGAGA GGCTAGCTACAACGA CCTGCGGA	14142
7156	GGAUCUCC G CCGGA AUG	5394	CATTCCGG GGCTAGCTACAACGA GGAGATCC	14143
7150	CCGCCGGA A UGGACACC	5395	GGTGTCCA GGCTAGCTACAACGA TCCGGCGG	14144
7146	CGGA AUGG A CACCUCUC	5396	GAGAGGTG GGCTAGCTACAACGA CCATTCCG	14145
7144	GAAUGGAC A CCUCUCUC	5397	GAGAGAGG GGCTAGCTACAACGA GTCCATTTC	14146
7133	UCUCUCUC A UCCUCCUC	5398	GAGGAGGA GGCTAGCTACAACGA GAGAGAGA	14147
7123	CCUCCUCC G CUCGAAGC	5399	GCTTCGAG GGCTAGCTACAACGA GGAGGAGG	14148
7116	CGCUCGAA G CGGGUCAA	5400	TTGACCCG GGCTAGCTACAACGA TTCGAGCG	14149
7112	CGAAGCGG G UCAAAAGA	5401	TCTTTTGA GGCTAGCTACAACGA CCGCTTCG	14150
7103	UCAAAAGA G UCCAGGGU	5402	ACCCTGGA GGCTAGCTACAACGA TCTTTTGA	14151
7096	AGUCCAGG G UAACUACC	5403	GTAGTTTA GGCTAGCTACAACGA CCTGGACT	14152
7093	CCAGGGUA A CUACCUUA	5404	TAAGTTAG GGCTAGCTACAACGA TACCCTGG	14153
7090	GGGUAAAU A CCUAUUC	5405	GAATAAGG GGCTAGCTACAACGA AGTTACCC	14154
7085	ACUACCUU A UUCUCUGA	5406	TCAGAGAA GGCTAGCTACAACGA AAGGTAGT	14155
7077	AUUCUCUG A CUCCACGC	5407	GCGTGGAG GGCTAGCTACAACGA CAGAGAAT	14156
7072	CUGACUCC A CGCGAGUG	5408	CACTCGCG GGCTAGCTACAACGA GGAGTCAG	14157
7070	GACUCCAC G CGAGUGAU	5409	ATCACTCG GGCTAGCTACAACGA GTGGAGTC	14158
7066	CCACGCGA G UGAUGUUA	5410	TAACATCA GGCTAGCTACAACGA TCGCGTGG	14159
7063	CGCGAGUG A UGUUACCG	5411	CGGTAACA GGCTAGCTACAACGA CACTCGCG	14160
7061	CGAGUGAU G UUACCGCC	5412	GGCGGTAA GGCTAGCTACAACGA ATCACTCG	14161
7058	GUGAUGUU A CCGCCCAU	5413	ATGGGCGG GGCTAGCTACAACGA AACATCAC	14162
7055	AUGUUAAC G CCAUCUC	5414	GAGATGGG GGCTAGCTACAACGA GGTAACAT	14163
7051	UACCGCCC A UCUCUGC	5415	GCAGGAGA GGCTAGCTACAACGA GGGCGGTA	14164
7044	CAUCUCCU G CCGCCACA	5416	TGTGGCGG GGCTAGCTACAACGA AGGAGATG	14165
7041	CUCCUGCC G CCACAGGA	5417	TCCTGTGG GGCTAGCTACAACGA GGCAGGAG	14166
7038	CUGCCGCC A CAGGAGGU	5418	ACCTCCTG GGCTAGCTACAACGA GCGGCGAG	14167
7031	CACAGGAG G UUGGCCUC	5419	GAGGCCAA GGCTAGCTACAACGA CTCCTGTG	14168
7027	GGAGGUUG G CCUCGAUG	5420	CATCGAGG GGCTAGCTACAACGA CAACCTCC	14169
7021	UGGCCUCG A UGAGGUCA	5421	TGACCTCA GGCTAGCTACAACGA CGAGGCCA	14170
7016	UCGAUGAG G UCAAAGUC	5422	GACTTTGA GGCTAGCTACAACGA CTCATCGA	14171
7010	AGGUCAAA G UCUGGGGA	5423	TCCCCAGA GGCTAGCTACAACGA TTTGACCT	14172
7001	UCUGGGGA G UCAUAUUG	5424	CAATATGA GGCTAGCTACAACGA TCCCCAGA	14173
6998	GGGGAGUC A UAUUGGGU	5425	ACCCAATA GGCTAGCTACAACGA GACTCCCC	14174

6996	GGAGUCAU A UUGGGUAA	5426	TTACCCAA GGCTAGCTACAACGA ATGACTCC	14175
6991	CAUAUUGG G UAAUGUAA	5427	ATACATTA GGCTAGCTACAACGA CCAATATG	14176
6988	AUUGGGUA A UGUUAUGUC	5428	GACATACA GGCTAGCTACAACGA TACCCAAT	14177
6986	UGGGUAAU G UAUGUCGC	5429	GCGACATA GGCTAGCTACAACGA ATTACCCA	14178
6984	GGUAUGU A UGUCGCCU	5430	AGGCGACA GGCTAGCTACAACGA ACATTACC	14179
6982	UAAUGUAA G UCGCCUUC	5431	GAAGGCGA GGCTAGCTACAACGA ATACATTA	14180
6979	UGUAUGUC G CCUUCGAA	5432	TTCGAAGG GGCTAGCTACAACGA GACATACA	14181
6966	CGAAGAAG G CGCAGACA	5433	TGTCTGCG GGCTAGCTACAACGA CTTCTTCG	14182
6964	AAGAAGGC G CAGACAGC	5434	GCTGTCTG GGCTAGCTACAACGA GCCTTCTT	14183
6960	AGGCGCAG A CAGCUGGC	5435	GCCAGCTG GGCTAGCTACAACGA CTGCGCCT	14184
6957	CGCAGACA G CUGGCUAG	5436	CTAGCCAG GGCTAGCTACAACGA TGTCTGCG	14185
6953	GACAGCUG G CUAGCUGA	5437	TCAGCTAG GGCTAGCTACAACGA CAGCTGTC	14186
6949	GCUGGCUA G CUGAGGAG	5438	CTCCTCAG GGCTAGCTACAACGA TAGCCAGC	14187
6941	GCUGAGGA G CUGGCCAA	5439	TTGGCCAG GGCTAGCTACAACGA TCCTCAGC	14188
6937	AGGAGCUG G CCAAGGAG	5440	CTCCTTGG GGCTAGCTACAACGA CAGCTCCT	14189
6921	GGGGGGAG A CCCCCUGG	5441	CCAGGGGG GGCTAGCTACAACGA CTCCCCC	14190
6913	ACCCCCUG G CCAGCCUA	5442	TAGGCTGG GGCTAGCTACAACGA CAGGGGGT	14191
6909	CCUGGCCA G CCUACGCU	5443	AGCGTAGG GGCTAGCTACAACGA TGGCCAGG	14192
6905	GCCAGCCU A CGCUUAGC	5444	GCTAAGCG GGCTAGCTACAACGA AGGCTGGC	14193
6903	CAGCCUAC G CUUAGCCG	5445	CGGCTAAG GGCTAGCTACAACGA GTAGCTGT	14194
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6895	GCUUAGCC G UCUCUCCU	5447	AGGAGAGA GGCTAGCTACAACGA GGCTAAGC	14196
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6883	CUCCUGUA A UGUGGGAG	5449	CTCCACCA GGCTAGCTACAACGA TACAGGAG	14198
6881	CCUGUAAU G UGGGAGGG	5450	CCCTCCCA GGCTAGCTACAACGA ATTACAGG	14199
6872	UGGGAGGG G UCGUGAG	5451	CTCACCAG GGCTAGCTACAACGA CCCTCCCA	14200
6868	AGGGGUCG G UGAGCAUG	5452	CATGCTCA GGCTAGCTACAACGA CGACCCCT	14201
6864	GUCGGUGA G CAUGGACG	5453	CGTCCATG GGCTAGCTACAACGA TCACCGAC	14202
6862	CGGUGAGC A UGGACGUG	5454	CACGTCCA GGCTAGCTACAACGA GCTCACCG	14203
6858	GAGCAUGG A CGUGAGCA	5455	TGCTCACG GGCTAGCTACAACGA CCATGCTC	14204
6856	GCAUGGAC G UGAGCACU	5456	AGTGCTCA GGCTAGCTACAACGA GTCCATGC	14205
6852	GGACGUGA G CACUGCUA	5457	TAGCAGTG GGCTAGCTACAACGA TCACGTCC	14206
6850	ACGUGAGC A CUGCUACA	5458	TGTAGCAG GGCTAGCTACAACGA GCTCACGT	14207
6847	UGAGCACU G CUACAUCC	5459	GGATGTAG GGCTAGCTACAACGA AGTGCTCA	14208
6844	GCACUGCU A CAUCCGGU	5460	ACCGGATG GGCTAGCTACAACGA AGCAGTGC	14209
6842	ACUGCUAC A UCCGGUUC	5461	GAACCGGA GGCTAGCTACAACGA GTAGCAGT	14210
6837	UACAUCCG G UUCGGGCU	5462	AGCCCGAA GGCTAGCTACAACGA CGGATGTA	14211
6831	CGGUUCGG G CUCGCAUG	5463	CATGCGAG GGCTAGCTACAACGA CCGAACCG	14212
6827	UCGGGCUC G CAUGGGAG	5464	CTCCCATG GGCTAGCTACAACGA GAGCCCGA	14213
6825	GGGCUCGC A UGGGAGCU	5465	AGCTCCCA GGCTAGCTACAACGA GCGAGCCC	14214
6819	GCAUGGGA G CUGUGACC	5466	GGTCACAG GGCTAGCTACAACGA TCCCATGC	14215
6816	UGGGAGCU G UGACCCAA	5467	TTGGGTCA GGCTAGCTACAACGA AGTCCCA	14216
6813	GAGCUGUG A CCCAACCA	5468	TGGTTGGG GGCTAGCTACAACGA CACAGCTC	14217
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6803	CCAACCAG G UAUUGGUU	5470	AACCAATA GGCTAGCTACAACGA CTGGTTGG	14219
6801	AACCAGGU A UUGGUUGA	5471	TCAACCAA GGCTAGCTACAACGA ACCTGGTT	14220
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6792	UUGGUUGA G CCCGACCU	5473	AGGTCGGG GGCTAGCTACAACGA TCAACCAA	14222
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6780	GACCUGGA A UGUGACCU	5475	AGGTCACA GGCTAGCTACAACGA TCCAGGTC	14224
6778	CCUGGAAU G UGACCUCC	5476	GGAGGTCA GGCTAGCTACAACGA ATTCCAGG	14225
6775	GGAAUGUG A CCUCCUCC	5477	GGAGGAGG GGCTAGCTACAACGA CACATTCC	14226
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6750	AGGUCCAC A CGCCGGAG	5481	CTCCGGCG GGCTAGCTACAACGA GTGGACCT	14230

6748	GUCCACAC G CCGGAGCG	5482	CGCTCCGG GGCTAGCTACAACGA GTGTGGAC	14231
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6740	GCCGGAGC G UUUCUGUG	5484	CACAGAAA GGCTAGCTACAACGA GCTCCGGC	14233
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6732	GUUUUCUGU G CAGGCGUA	5486	TACGCCTG GGCTAGCTACAACGA ACAGAAAC	14235
6728	CUGUGCAG G CGUACCCC	5487	GGGGTACG GGCTAGCTACAACGA CTGCACAG	14236
6726	GUGCAGGC G UACCCCAU	5488	ATGGGGTA GGCTAGCTACAACGA GCCTGCAC	14237
6724	GCAGGCGU A CCCCAUCC	5489	GGATGGGG GGCTAGCTACAACGA ACGCCTGC	14238
6719	CGUACCCC A UCCACUUC	5490	GAAGTGGA GGCTAGCTACAACGA GGGGTACG	14239
6715	CCCAUCC A CUUCCGUG	5491	CACGGAAG GGCTAGCTACAACGA GGATGGGG	14240
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6683	GGAACCUG G CACGGGCA	5496	TGCCCCTG GGCTAGCTACAACGA CAGGTTCC	14245
6681	AACCUGGC A CGGGCAUU	5497	AATGCCCG GGCTAGCTACAACGA GCCAGGTT	14246
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6658	UGUCAGUG G UCAUGCCC	5504	GGGCATGA GGCTAGCTACAACGA CACTGACA	14253
6655	CAGUGGUC A UGCCCGUC	5505	GACGGGCA GGCTAGCTACAACGA GACCACTG	14254
6653	GUGGUCAU G CCCGUCAC	5506	GTGACGGG GGCTAGCTACAACGA ATGACCAC	14255
6649	UCAUGCCC G UCACGUAG	5507	CTACGTGA GGCTAGCTACAACGA GGGCATGA	14256
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6619	CCCGGUA A CCUCCACG	5515	CGTGGAGG GGCTAGCTACAACGA TACGCGGG	14264
6613	UAACCUCC A CGUACUCC	5516	GGAGTACG GGCTAGCTACAACGA GGAGGTTA	14265
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6595	CAGCGGCC A CCCGCCAU	5521	ATGGCGGG GGCTAGCTACAACGA GGCCGCTG	14270
6591	GGCCACCC G CCAUAGCG	5522	CGCTATGG GGCTAGCTACAACGA GGGTGGCC	14271
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6585	CCGCCAUA G CGCCCUAG	5524	CTAGGGCG GGCTAGCTACAACGA TATGGCGG	14273
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6575	GCCCUAGA A UAGUUGG	5526	CCAAACTA GGCTAGCTACAACGA TCTAGGGC	14275
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6319	GAAGCCAG G UCUUGAAG	5590	CTTCAAGA GGCTAGCTACAACGA CTGGCTTC	14339
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6242	GUGGAGCA G UCCUCAU	5610	AATGAGGA GGCTAGCTACAACGA TGCTCCAC	14359
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6224	AUCCACUG A UGGAGCCU	5614	AGGCTCCA GGCTAGCTACAACGA CAGTGGAT	14363
6219	CUGAUGGA G CCUCCUCA	5615	TGAGGAGG GGCTAGCTACAACGA TCCATCAG	14364
6210	CCUCCUCA G CAGCUGAG	5616	CTCAGCTG GGCTAGCTACAACGA TGAGGAGG	14365
6207	CCUCAGCA G CUGAGUGA	5617	TCAGTCA GGCTAGCTACAACGA TGCTGAGG	14366
6202	GCAGCUGA G UGAUGGUG	5618	CACCATCA GGCTAGCTACAACGA TCAGCTGC	14367
6199	GCUGAGUG A UGGUGAGG	5619	CCTACCA GGCTAGCTACAACGA CACTCAGC	14368
6196	GAGUGAUG G UGAGGUG	5620	CAGCCTCA GGCTAGCTACAACGA CATCACTC	14369
6191	AUGGUGAG G CUGGAGAG	5621	CTCTCCAG GGCTAGCTACAACGA CTCACCAT	14370
6181	UGGAGAGG A UUUGUGUG	5622	CACACAAA GGCTAGCTACAACGA CCTCTCCA	14371
6177	GAGGAUUU G UGUGACGC	5623	GCGTCACA GGCTAGCTACAACGA AAATCCTC	14372
6175	GGAUUUGU G UGACGCGC	5624	GCGCGTCA GGCTAGCTACAACGA ACAATATC	14373
6172	UUUGUGUG A CGCGCGCC	5625	GGCGCGCG GGCTAGCTACAACGA CACACAAA	14374
6170	UGUGUGAC G CGCGCGC	5626	GCGCGCGG GGCTAGCTACAACGA GTCACACA	14375
6168	UGUGACGC G CGCGCUG	5627	CAGCGCGG GGCTAGCTACAACGA GCGTCACA	14376
6166	UGACGCGC G CCGCUGCG	5628	CGCAGCGG GGCTAGCTACAACGA GCGGCTCA	14377
6163	CGCGCGCC G CUGCGUCG	5629	CGACGCAG GGCTAGCTACAACGA GGCGCGCG	14378
6160	GCGCGCGU G CGUCGCUC	5630	GAGCGACG GGCTAGCTACAACGA AGCGGCGC	14379
6158	GCCGCGUC G UCGCUCUC	5631	GAGAGCGA GGCTAGCTACAACGA GCAGCGGC	14380
6155	GCUGCGUC G CUCUCAGG	5632	CCTGAGAG GGCTAGCTACAACGA GACGCAGC	14381
6147	GCUCUCAG G CACAUAGU	5633	ACTATGTG GGCTAGCTACAACGA CTGAGAGC	14382
6145	UCUCAGGC A CAUAGUGC	5634	GCACTATG GGCTAGCTACAACGA GCCTGAGA	14383
6143	UCAGGCAC A UAGUGCGU	5635	ACGCACTA GGCTAGCTACAACGA GTGCTGA	14384
6140	GGCACAUA G UGCGUGGG	5636	CCACGCA GGCTAGCTACAACGA TATGTGCC	14385
6138	CACAUAGU G CGUGGGGG	5637	CCCCCAG GGCTAGCTACAACGA ACTATGTG	14386
6136	CAUAGUGC G UGGGGGAG	5638	CTCCCCCA GGCTAGCTACAACGA GCACTATG	14387
6127	UGGGGGAG A CAUGGUUG	5639	CAACCATG GGCTAGCTACAACGA CTCCCCCA	14388
6125	GGGGAGAC A UGGUUGCC	5640	GGCAACCA GGCTAGCTACAACGA GTCTCCCC	14389
6122	GAGACAUG G UUGCCCCG	5641	CGGGGCAA GGCTAGCTACAACGA CATGTCTC	14390
6119	ACAUGGUU G CCCCAGCA	5642	TCGCGGGG GGCTAGCTACAACGA AACCATGT	14391
6114	GUUGCCCC G CGAAGCGA	5643	TCGCTTCG GGCTAGCTACAACGA GGGGCAAC	14392
6109	CCCGCGAA G CGAAGCGU	5644	AGCGTTTC GGCTAGCTACAACGA TTCGCGGG	14393
6105	CGAAGCGA A CGCUAUA	5645	TGATAGCG GGCTAGCTACAACGA TCGTTTCG	14394
6103	AAGCGAAC G CUAUCAGC	5646	GCTGATAG GGCTAGCTACAACGA GTTCGCTT	14395
6100	CGAAGCGU A UCAGCCGA	5647	TCGGCTGA GGCTAGCTACAACGA AGCGTTCG	14396
6096	CGCUAUA G CCGAUUCA	5648	TGAATCGG GGCTAGCTACAACGA TGATAGCG	14397
6092	AUCAGCCG A UUCAUCCA	5649	TGGATGAA GGCTAGCTACAACGA CGGCTGAT	14398

6088	GCCGAUUC A UCCACUGC	5650	GCACTGGA GGCTAGCTACAACGA GAATCGGC	14399
6084	AUUCAUCC A CUGCACAG	5651	CTGTGCAG GGCTAGCTACAACGA GGATGAAT	14400
6081	CAUCCACU G CACAGCGC	5652	GCGCTGTG GGCTAGCTACAACGA AGTGGATG	14401
6079	UCCACUGC A CAGCGCCC	5653	GGGCGCTG GGCTAGCTACAACGA GCAGTGGA	14402
6076	ACUGCACA G CGCCUCU	5654	AGAGGGCG GGCTAGCTACAACGA TGTGCAGT	14403
6074	UGCACAGC G CCCUCUCC	5655	GGAGAGGG GGCTAGCTACAACGA GCTGTGCA	14404
6062	UCUCCUGG G CCCACAUG	5656	CATGTGGG GGCTAGCTACAACGA CCAGGAGA	14405
6058	CUGGGCCC A CAUGCCGA	5657	TCGGCATG GGCTAGCTACAACGA GGGCCCAG	14406
6056	GGGCCCAC A UGCCGACG	5658	CGTCGGCA GGCTAGCTACAACGA GTGGGCCC	14407
6054	GCCCACAU G CCGACGCA	5659	TGCGTCGG GGCTAGCTACAACGA ATGTGGGC	14408
6050	ACAUGCCG A CGCAGUUA	5660	ATACTGCG GGCTAGCTACAACGA CGGCATGT	14409
6048	AUGCCGAC G CAGUAUCG	5661	CGATACTG GGCTAGCTACAACGA GTCGGCAT	14410
6045	CCGACGCA G UAUCGCU	5662	CAGCGATA GGCTAGCTACAACGA TGCGTCGG	14411
6043	GACGCAGU A UCGCUGCG	5663	CGCAGCGA GGCTAGCTACAACGA ACTGCGTC	14412
6040	GCAGUAUC G CUGCGCAC	5664	GTGCGCAG GGCTAGCTACAACGA GATACTGC	14413
6037	GUAUCGCU G CGCACACC	5665	GGTGTGCG GGCTAGCTACAACGA AGCGATAC	14414
6035	AUCGCGC A CACACCAC	5666	GTGGTGTG GGCTAGCTACAACGA GCAGCGAT	14415
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6031	CUGCGCAC A CCACCCCG	5668	CGGGGTGG GGCTAGCTACAACGA GTGCGCAG	14417
6028	CGCACACC A CCCCACG	5669	CGTCGGGG GGCTAGCTACAACGA GGTGTGCG	14418
6022	CCACCCCG A CGACCAGG	5670	CCTGGTCG GGCTAGCTACAACGA CGGGGTGG	14419
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6013	CGACCAGG G CGCCAGGA	5672	TCCTGGCG GGCTAGCTACAACGA CCTGGTCG	14421
6011	ACCAGGGG G CCAGGAGA	5673	TCTCCTGG GGCTAGCTACAACGA GCCCTGGT	14422
5998	GAGAGAGG A UGGCAGGG	5674	CCCTGCCA GGCTAGCTACAACGA CCTCTCTC	14423
5995	AGAGGAUG G CAGGGAGU	5675	ACTCCCTG GGCTAGCTACAACGA CATCTCT	14424
5988	GGCAGGGA G UAAGUUGA	5676	TCAACTTA GGCTAGCTACAACGA TCCCTGCC	14425
5984	GGGAGUAA G UUGACCAG	5677	CTGGTCAA GGCTAGCTACAACGA TTACTCCC	14426
5980	GUAAGUUG A CCAGGUCC	5678	GGACCTGG GGCTAGCTACAACGA CAACTTAC	14427
5975	UUGACCAG G UCCUCGGU	5679	ACCGAGGA GGCTAGCTACAACGA CTGGTCAA	14428
5968	GGUCCUCG G UAGAAGGC	5680	GCCTTCTA GGCTAGCTACAACGA CGAGGACC	14429
5961	GGUAGAAG G CAUCUCCC	5681	GGGAGATG GGCTAGCTACAACGA CTTCTACC	14430
5959	UAGAAGG A UCUCCCCG	5682	CGGGGAGA GGCTAGCTACAACGA GCCTTCTA	14431
5951	AUCUCCCC G CCAUGAC	5683	GTATAGAG GGCTAGCTACAACGA GGGGAGAT	14432
5947	CCCCGCUC A UGACCUUG	5684	CAAGGTCA GGCTAGCTACAACGA GAGCGGGG	14433
5944	CGCUCAUG A CCUUGAAG	5685	CTTCAAGG GGCTAGCTACAACGA CATGAGCG	14434
5935	CCUUGAAG G CCACGAGA	5686	TCTCGTGG GGCTAGCTACAACGA CTTCAAGG	14435
5932	UGAAGGCC A CGAGAGCA	5687	TGCTCTCG GGCTAGCTACAACGA GGCCTTCA	14436
5926	CCACGAGA G CACCCGCC	5688	GGCGGGTG GGCTAGCTACAACGA TCTCGTGG	14437
5924	ACGAGAGC A CCCGCCAC	5689	GTGGCGGG GGCTAGCTACAACGA GCTCTCGT	14438
5920	GAGCACCC G CCACUCCU	5690	AGGAGTGG GGCTAGCTACAACGA GGGTGCTC	14439
5917	CACCCGCC A CUCCUGCU	5691	AGCAGGAG GGCTAGCTACAACGA GCGGGTGG	14440
5911	CCACUCCU G CUCCAUG	5692	CTATGGAG GGCTAGCTACAACGA AGGAGTGG	14441
5906	CCUGCUCC A UAGCCCGC	5693	GCGGGCTA GGCTAGCTACAACGA GGAGCAGG	14442
5903	GCUCCAUA G CCCGCCAG	5694	CTGGCGGG GGCTAGCTACAACGA TATGGAGC	14443
5899	CAUAGCCC G CCAGAAUG	5695	CATTCTGG GGCTAGCTACAACGA GGGCTATG	14444
5893	CCGCCAGA A UGUUACA	5696	TGTAGACA GGCTAGCTACAACGA TCTGGCGG	14445
5891	GCCAGAAU G UCUAACA	5697	CTTGTAGA GGCTAGCTACAACGA ATTCTGGC	14446
5887	GAAUGUCU A CAAGCACC	5698	GTGCTTGG GGCTAGCTACAACGA AGACATT	14447
5883	GUCUACAA G CACCUUCC	5699	GGAAGGTG GGCTAGCTACAACGA TTGTAGAC	14448
5881	CUACAAGC A CCUCCCA	5700	TGGGAAGG GGCTAGCTACAACGA GCTGTAG	14449
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5864	AGGCCUAU G CUGCCAAC	5703	GTTGGCAG GGCTAGCTACAACGA ATAGGCCT	14452
5861	CCUAUGCU G CCAACAGC	5704	GCTGTTGG GGCTAGCTACAACGA AGCATAGG	14453
5857	UGCUGCCA A CAGCCGCG	5705	CGCGGCTG GGCTAGCTACAACGA TGGCAGCA	14454

5854	UGCCAACA G CCGCGCCA	5706	TGGCGCGG GGCTAGCTACAACGA TGTGGCA	14455
5851	CAACAGCC G CGCCAGCG	5707	CGCTGGCG GGCTAGCTACAACGA GGCTGTTG	14456
5849	ACAGCCGC G CAGCGAU	5708	ATCGCTGG GGCTAGCTACAACGA GCGGCTGT	14457
5845	CCGCGCCA G CGAUGCCG	5709	CGGCATCG GGCTAGCTACAACGA TGGCGCGG	14458
5842	CGCCAGCG A UGCCGGCG	5710	CGCCGGCA GGCTAGCTACAACGA CGCTGGCG	14459
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5836	CGAUGCCG G CGCCACG	5712	CGTGGGCG GGCTAGCTACAACGA CGGCATCG	14461
5834	AUGCCGGC G CCCACGAA	5713	TTCGTGGG GGCTAGCTACAACGA GCCGGCAT	14462
5830	CGGCGCCC A CGAAGGCC	5714	GGCCTTCG GGCTAGCTACAACGA GGGCGCCG	14463
5824	CCACGAAG G CCGAAACG	5715	CGTTTCGG GGCTAGCTACAACGA CTTCGTGG	14464
5818	AGGCCGAA A CGGCUCUG	5716	CAGAGCCG GGCTAGCTACAACGA TTCGGCCT	14465
5815	CCGAAACG G CUCUGGGG	5717	CCCCAGAG GGCTAGCTACAACGA CGTTTCGG	14466
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5794	CGAGUUGG G CGGCCACC	5720	GGTGGCCG GGCTAGCTACAACGA CCAACTCG	14469
5791	GUUGGGCG G CCACCCAC	5721	GTGGGTGG GGCTAGCTACAACGA CGCCCAAC	14470
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5771	CCCAAGAU G UUGAACAG	5725	CTGTTCAA GGCTAGCTACAACGA ATCTGGG	14474
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5756	AGGAGGGU G CUUUGGGU	5728	ACCCAAAG GGCTAGCTACAACGA ACCCTCCT	14477
5749	UGCUUUGG G UGUGAGC	5729	GCTCACCA GGCTAGCTACAACGA CCAAAGCA	14478
5746	UUUGGGUG G UGAGCGG	5730	CCCGCTCA GGCTAGCTACAACGA CACCCAA	14479
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5738	GUGAGCGG G CUGUGAU	5732	ATCACCAG GGCTAGCTACAACGA CCGCTCAC	14481
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5731	GGCUGGUG A UGGAGGCU	5734	AGCCTCCA GGCTAGCTACAACGA CACCAGCC	14483
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5713	UGAUGCC A UCAAUGAU	5739	ATCATTTA GGCTAGCTACAACGA GGCATTCA	14488
5709	UGCAUCA A UGAUGCUA	5740	TAGATCA GGCTAGCTACAACGA TGATGGCA	14489
5706	CAUCAAU G UGCUAUCG	5741	CGATAGCA GGCTAGCTACAACGA CATTGATG	14490
5704	UCAUGAU G CUAUCGCG	5742	CGCGATAG GGCTAGCTACAACGA ATCATTGA	14491
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5698	AUGCUAUC G CGGGGUUC	5744	GAACCCCG GGCTAGCTACAACGA GATAGCAT	14493
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5680	CAGGCAGA G UGACAAG	5747	CTTGTTCA GGCTAGCTACAACGA TCTGCCTG	14496
5676	CAGAGUGG A CAAGCCUG	5748	CAGGCTTG GGCTAGCTACAACGA CCACTCTG	14497
5672	GUGGACAA G CCUGCUAG	5749	CTAGCAGG GGCTAGCTACAACGA TTGTCCAC	14498
5668	ACAAGCCU G CUAGGUAC	5750	GTACCTAG GGCTAGCTACAACGA AGGCTTGT	14499
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5656	GGUACUGU A UCCCGCUG	5754	CAGCGGGA GGCTAGCTACAACGA ACAGTACC	14503
5651	UGUAUCCC G CUGAUGAA	5755	TTCATCAG GGCTAGCTACAACGA GGGATACA	14504
5647	UCCCGCUG A UGAAAUUC	5756	GAATTTCA GGCTAGCTACAACGA CAGCGGGA	14505
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5633	UUCCACAU G UGUUCGC	5760	GCGAAGCA GGCTAGCTACAACGA ATGTGGAA	14509
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5617	CCCAGAAA G CCUCAAGG	5763	CCTTGAGG GGCTAGCTACAACGA TTTCTGGG	14512
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5590	UGGAUUC A CCACGGGA	5768	TCCCGTGG GGCTAGCTACAACGA GGAATCCA	14517
5587	AUUCACC A CGGGAGCA	5769	TGCTCCCG GGCTAGCTACAACGA GGTGGAAT	14518
5581	CCACGGGA G CAGCAGCC	5770	GGCTGCTG GGCTAGCTACAACGA TCCCGTGG	14519
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5575	GAGCAGCA G CCUCCGCU	5772	AGCGGAGG GGCTAGCTACAACGA TGCTGCTC	14521
5569	CAGCCUCC G CUUGGUUG	5773	CAACCAAG GGCTAGCTACAACGA GGAGGCTG	14522
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5554	UGGUGGCU G UUUGCAGC	5777	GCTGCAA GGCTAGCTACAACGA AGCCACCA	14526
5550	GGCUGUUU G CAGCAAUC	5778	GATTGCTG GGCTAGCTACAACGA AAACAGCC	14527
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5544	UUGCAGCA A UCGAGCG	5780	CGTCGGA GGCTAGCTACAACGA TGCTGCAA	14529
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5536	AUCCGAGC G CCUUCUGC	5782	GCAGAAGG GGCTAGCTACAACGA GCTCGGAT	14531
5529	CGCCUUCU G CUUGAACU	5783	AGTTCAGG GGCTAGCTACAACGA AGAAGGCG	14532
5523	CUGCUUGA A CUGCUCGG	5784	CCGAGCAG GGCTAGCTACAACGA TCAAGCAG	14533
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5515	ACUGCUCG G CGAGCUGC	5786	GCAGCTCG GGCTAGCTACAACGA CGAGCAGT	14535
5511	CUCGGCGA G CUGCAUCC	5787	GGATGCAG GGCTAGCTACAACGA TCGCCGAG	14536
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5506	CGAGCUGC A UCCCCUGU	5789	ACAGGGGA GGCTAGCTACAACGA GCAGCTCG	14538
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5454	CUCAUCGA A CUCCUGGU	5800	ACCAGGAG GGCTAGCTACAACGA TCGATGAG	14549
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5432	GCCUCCCU G UCGGGGAU	5803	ATCCCCGA GGCTAGCTACAACGA AGGGAGGC	14552
5425	UGUCGGGG A UAACAGCC	5804	GGCTGTTA GGCTAGCTACAACGA CCCCACA	14553
5422	CGGGGAUA A CAGCCGGC	5805	GCCGGCTG GGCTAGCTACAACGA TATCCCCG	14554
5419	GGUAACA G CCGGCUUC	5806	GAAGCCGG GGCTAGCTACAACGA TGTATATCC	14555
5415	AACAGCCG G CUUCCCGG	5807	CCGGGAAG GGCTAGCTACAACGA CGGCTGTT	14556
5406	CUUCCCGG A CAAGAUGA	5808	TCATCTTG GGCTAGCTACAACGA CCGGAAG	14557
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5398	ACAAGAUG A UUCUGCCC	5810	GGGCAGAA GGCTAGCTACAACGA CATCTTGT	14559
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5389	UUCUGCCC A CAAUGACC	5812	GGTCATTG GGCTAGCTACAACGA GGCAGAA	14561
5386	UGCCCA A UGACCACG	5813	CGTGGTCA GGCTAGCTACAACGA TGTGGGCA	14562
5383	CCACAAUG A CCACGCUG	5814	CAGCGTGG GGCTAGCTACAACGA CATGTGG	14563
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5375	ACCACGCU G CCUGUCGU	5817	ACGACAGG GGCTAGCTACAACGA AGCGTGGT	14566

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5315	ACCCAGGU G CUGUGAC	5834	GTCACCAG GGCTAGCTACAACGA ACCTGGGT	14583
5311	AGGUGCUG G UGACGACC	5835	GGTCGTCA GGCTAGCTACAACGA CAGCACCT	14584
5308	UGCUGGUG A CGACCUCC	5836	GGAGGTCG GGCTAGCTACAACGA CACCAGCA	14585
5305	UGGUGACG A CCUCCAGG	5837	CCTGGAGG GGCTAGCTACAACGA CGTCACCA	14586
5297	ACCUCCAG G UCAGCCGA	5838	TCGGGTGA GGCTAGCTACAACGA CTGGAGGT	14587
5293	CCAGGUCA G CCGACAUG	5839	CATGTCGG GGCTAGCTACAACGA TGACCTGG	14588
5289	GUCAGCCG A CAUGCAUG	5840	CATGCATG GGCTAGCTACAACGA CGGCTGAC	14589
5287	CAGCCGAC A UGCAUGUC	5841	GACATGCA GGCTAGCTACAACGA GTCGGCTG	14590
5285	GCCGACAU G CAUGUCAU	5842	ATGACATG GGCTAGCTACAACGA ATGTCGGC	14591
5283	CGACAUGC A UGUCAUGA	5843	TCATGACA GGCTAGCTACAACGA GCATGTCG	14592
5281	ACAUGCAU G UCAUGAUG	5844	CATCATGA GGCTAGCTACAACGA ATGCATGT	14593
5278	UGCAUGUC A UGAUGUUA	5845	ATACATCA GGCTAGCTACAACGA GACATGCA	14594
5275	AUGUCAUG A UGUUUUG	5846	CAAATACA GGCTAGCTACAACGA CATGACAT	14595
5273	GUCAUGAU G UAUUUGGU	5847	ACCAAATA GGCTAGCTACAACGA ATCATGAC	14596
5271	CAUGAUGU A UUUGGUUA	5848	TAACCAAA GGCTAGCTACAACGA ACATCATG	14597
5266	UGUAUUUG G UUAUGGGG	5849	CCCCATA GGCTAGCTACAACGA CAAATACA	14598
5263	AUUUGGUU A UGGGGUGU	5850	ACACCCCA GGCTAGCTACAACGA AACCAAT	14599
5258	GUUAUGGG G UGUGAGAG	5851	CTCACACA GGCTAGCTACAACGA CCCATAAC	14600
5256	UAUGGGGU G UGUGAGGG	5852	CCCTCACA GGCTAGCTACAACGA ACCCATA	14601
5254	UGGGGUGU G UGAGGGUG	5853	CACCCCTCA GGCTAGCTACAACGA ACACCCCA	14602
5248	GUGUGAGG G UGACAUCA	5854	TGATGTCA GGCTAGCTACAACGA CCTCACAC	14603
5245	UGAGGGUG A CAUCAUUU	5855	AAATGATG GGCTAGCTACAACGA CACCCCTCA	14604
5243	AGGGUGAC A UCAUUUUG	5856	CAAAATGA GGCTAGCTACAACGA GTCACCCT	14605
5240	GUGACAUC A UUUUGGAC	5857	GTCCAAA GGCTAGCTACAACGA GATGTCAC	14606
5233	CAUUUUGG A CGGCUCCU	5858	AGGAGCCG GGCTAGCTACAACGA CCAAAATG	14607
5230	UUUGGACG G CUCCUAGC	5859	GCTAGGAG GGCTAGCTACAACGA CGTCCAAA	14608
5223	GGCUCCUA G CCUAUACA	5860	TGTATAGG GGCTAGCTACAACGA TAGGAGCC	14609
5219	CCUAGCCU A UACAGCAG	5861	CTGCTGTA GGCTAGCTACAACGA AGGCTAGG	14610
5217	UAGCCUUA A CAGCAGGG	5862	CCCTGCTG GGCTAGCTACAACGA ATAGGCTA	14611
5214	CCUAUACA G CAGGGGUG	5863	CACCCCTG GGCTAGCTACAACGA TGTATAGG	14612
5208	CAGCAGGG G UGUUGGCC	5864	GGCCAACA GGCTAGCTACAACGA CCCTGCTG	14613
5206	GCAGGGGU G UUGGCCCG	5865	CGGGCCAA GGCTAGCTACAACGA ACCCTGCT	14614
5202	GGGUGUUG G CCCGUGUA	5866	TACACGGG GGCTAGCTACAACGA CAACACCC	14615
5198	GUUGGCCC G UGUAGCGU	5867	ACGCTACA GGCTAGCTACAACGA GGGCCAAC	14616
5196	UGGCCCCU G UAGCGUAG	5868	CTACGCTA GGCTAGCTACAACGA ACGGCCCA	14617
5193	CCCUGUUA G CGUAGGCU	5869	AGCCTACG GGCTAGCTACAACGA TACACGGG	14618
5191	CGUGUAGC G UAGGCUUU	5870	AAAGCCTA GGCTAGCTACAACGA GCTACACG	14619
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5181	AGGCUUUA G CCGUGUGA	5872	TCACACGG GGCTAGCTACAACGA TAAAGCCT	14621
5178	CUUUAGCC G UGUGAGAC	5873	GTCTCACA GGCTAGCTACAACGA GGCTAAAG	14622

5176	UUAGCCGU G UGAGACAC	5874	GTGTCTCA GGCTAGCTACAACGA ACGGCTAA	14623
5171	CGUGUGAG A CACUCCA	5875	TGGAAGTG GGCTAGCTACAACGA CTCACACG	14624
5169	UGUGAGAC A CUUCCACA	5876	TGTGGAAG GGCTAGCTACAACGA GTCTCACA	14625
5163	ACACUUC A CAUUUGAU	5877	ATCAAATG GGCTAGCTACAACGA GGAAGTGT	14626
5161	ACUUCCAC A UUUGAUCC	5878	GGATCAA GGCTAGCTACAACGA GTGGAAGT	14627
5156	CACAUUUG A UCCCACGA	5879	TCGTGGGA GGCTAGCTACAACGA CAAATGTG	14628
5151	UUGAUCCC A CGAUGGGG	5880	CCCCATCG GGCTAGCTACAACGA GGGATCAA	14629
5148	AUCCACG A UGGGGUG	5881	CACCCCA GGCTAGCTACAACGA CGTGGGAT	14630
5142	CGAUGGGG G UGAGCCU	5882	AGGCTCCA GGCTAGCTACAACGA CCCATCG	14631
5137	GGGUGGA G CCUGAGCC	5883	GGCTCAGG GGCTAGCTACAACGA TCCACCCC	14632
5131	GAGCCUGA G CCCUGGCG	5884	CGCCAGGG GGCTAGCTACAACGA TCAGGCTC	14633
5125	GAGCCUG G CGCACACU	5885	AGTGTGCG GGCTAGCTACAACGA CAGGGCTC	14634
5123	GCCCUGGC G CACACUGU	5886	ACAGTGTG GGCTAGCTACAACGA GCCAGGGC	14635
5121	CCUGGCGC A CACUGUGG	5887	CCACAGTG GGCTAGCTACAACGA GCGCCAGG	14636
5119	UGGCGCAC A CUGUGGCU	5888	AGCCACAG GGCTAGCTACAACGA GTGCGCCA	14637
5116	CGCACACU G UGGCUUGG	5889	CCAAGCCA GGCTAGCTACAACGA AGTGTGCG	14638
5113	ACACUGG G CUUGGUU	5890	ATACCAAG GGCTAGCTACAACGA CACAGTGT	14639
5108	GUGGCUUG G UAUGCUAC	5891	GTAGCATA GGCTAGCTACAACGA CAAGCCAC	14640
5106	GGCUUGGU A UGCUACCA	5892	TGGTAGCA GGCTAGCTACAACGA ACCAAGCC	14641
5104	CUUGGUU G CUACCAGG	5893	CCTGGTAG GGCTAGCTACAACGA ATACCAAG	14642
5101	GGUAGCU A CCAGGUAG	5894	CTACCTGG GGCTAGCTACAACGA AGCATACC	14643
5096	GCUACCAG G UAGGGGAG	5895	CTCCCTTA GGCTAGCTACAACGA CTGGTAGC	14644
5087	UAGGGGAG G UUUUCUCC	5896	GGAGAAA GGCTAGCTACAACGA CTCCCTTA	14645
5077	UUUCUCCU G CCUGCUUG	5897	CAAGCAGG GGCTAGCTACAACGA AGGAGAAA	14646
5073	UCCUGCCU G CUUGGUCU	5898	AGACCAAG GGCTAGCTACAACGA AGGCAGGA	14647
5068	CCUGCUUG G UCUGGGAC	5899	GTCCAGA GGCTAGCTACAACGA CAAGCAGG	14648
5061	GGUCUGGG A CAAGAAGU	5900	ACTTCTTG GGCTAGCTACAACGA CCCAGACC	14649
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5050	AGAAGUGG G CAUCUAUG	5902	CATAGATG GGCTAGCTACAACGA CCACTTCT	14651
5048	AAGUGGGC A UCUAUGUG	5903	CACATAGA GGCTAGCTACAACGA GCCCACTT	14652
5044	GGGCAUCU A UGUGGGUG	5904	CACCCACA GGCTAGCTACAACGA AGATGCC	14653
5042	GCAUCUAU G UGGUGAG	5905	CTCACCCA GGCTAGCTACAACGA ATAGATGC	14654
5038	CUAUGUGG G UGAGCCU	5906	AGGCCTCA GGCTAGCTACAACGA CCACATAG	14655
5033	UGGUGAG G CCUGUGAA	5907	TTCAACAGG GGCTAGCTACAACGA CTCACCA	14656
5029	UGAGCCU G UGAAGACA	5908	TGTCTTCA GGCTAGCTACAACGA AGGCCTCA	14657
5023	CUGUGAAG A CACCCUCC	5909	GGAGGGTG GGCTAGCTACAACGA CTTACAG	14658
5021	GUGAAGAC A CCCUCCA	5910	TGGGAGGG GGCTAGCTACAACGA GTCTTCAC	14659
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4983	GAAGGGCA A CCCUGGUG	5916	CACCAGGG GGCTAGCTACAACGA TGCCCTTC	14665
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4975	ACCCUGGU G UAUUAGG	5918	CCTAAATA GGCTAGCTACAACGA ACCAGGGT	14667
4973	CCUGGUGU A UUUAGGUA	5919	TACCTAAA GGCTAGCTACAACGA ACACCAGG	14668
4967	GUUUUAG G UAAGCCCG	5920	CGGGCTTA GGCTAGCTACAACGA CTAAATAC	14669
4963	UUAGGUAA G CCCGCAAC	5921	GTTGCGGG GGCTAGCTACAACGA TTACCTAA	14670
4959	GUUAGCCC G CAACCUAA	5922	TTAGGTTG GGCTAGCTACAACGA GGGCTTAC	14671
4956	AGCCCGCA A CCUACGG	5923	CCGTTAGG GGCTAGCTACAACGA TGCGGGCT	14672
4951	GCAACCUA A CGGAGGUC	5924	GACCTCCG GGCTAGCTACAACGA TAGGTTGC	14673
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4939	AGGUCUCG G CGGGCGUG	5926	CACGCCCG GGCTAGCTACAACGA CGAGACCT	14675
4935	CUCGGCGG G CGUGAGCU	5927	AGCTCACG GGCTAGCTACAACGA CCGCCGAG	14676
4933	CGGCGGGC G UGAGCUCG	5928	CGAGCTCA GGCTAGCTACAACGA GCCCGCCG	14677
4929	GGGCGUGA G CUCGUACC	5929	GGTACGAG GGCTAGCTACAACGA TCACGCC	14678

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4916	UACCAAGC A CAUCCCGC	5933	GCGGGATG GGCTAGCTACAACGA GCTTGGTA	14682
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4895	UAGCACUC A CACAGGAC	5940	GTCCTGTG GGCTAGCTACAACGA GAGTGCTA	14689
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4871	UCGAACAU G CCCGAAGG	5946	CCTTCGGG GGCTAGCTACAACGA ATGTTCTA	14695
4863	GCCCGAAG G CCGCUCUC	5947	GAGAGCGG GGCTAGCTACAACGA CTTCGGGC	14696
4860	CGAAGGCC G CUCUCCUG	5948	CAGGAGAG GGCTAGCTACAACGA GGCCTTCG	14697
4849	CUCCUGGA G UCACAAAC	5949	GTTTGTGA GGCTAGCTACAACGA TCCAGGAG	14698
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4781	GACACUGC G UCUUGGGG	5966	CCCCAAGA GGCTAGCTACAACGA GCAGTGTC	14715
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4771	CUUGGGGC A CGGUCGUC	5968	GACGACCG GGCTAGCTACAACGA GCCCCAAG	14717
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4765	GCACGGUC G UCGUCUCA	5970	TGAGACGA GGCTAGCTACAACGA GACCGTGC	14719
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4511	AAGAUGAG A UGCCUCCC	6036	GGGAGGCA GGCTAGCTACAACGA CTCATCTT	14785
4509	GAUGAGAU G CCUCCCCC	6037	GGGGGAGG GGCTAGCTACAACGA ATCTCATC	14786
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4486	UGGUCUCG A UGGGAUG	6040	CATCCCCA GGCTAGCTACAACGA CGAGACCA	14789
4480	CGAUGGGG A UGGCUUUG	6041	CAAAGCCA GGCTAGCTACAACGA CCCCATCG	14790

4477	UGGGGAUG G CUUUGCCA	6042	TGGCAAAG GGCTAGCTACAACGA CATCCCCA	14791
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4448	UCUCCGGU G UUGGACAA	6047	TTGTCCAA GGCTAGCTACAACGA ACCGAGAG	14796
4443	GGUGUUGG A CAAGGCUA	6048	TAGCCTTG GGCTAGCTACAACGA CCAACACC	14797
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4435	ACAAGGCU A UCUCUCCG	6050	CGAGGAGA GGCTAGCTACAACGA AGCCTTGT	14799
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4424	UCCUCGAU G UUGGGAUG	6052	CATCCCAA GGCTAGCTACAACGA ATCGAGGA	14801
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4408	GUGGCACG G UGACCGAU	6057	ATCGGTCA GGCTAGCTACAACGA CGTGCCAC	14806
4405	GCACGGUG A CCGAUCCC	6058	GGGATCGG GGCTAGCTACAACGA CACCGTGC	14807
4401	GGUGACCG A UCCCGGAG	6059	CTCCGGGA GGCTAGCTACAACGA CGGTCAAC	14808
4392	UCCCGGAG G CGUAGCGG	6060	CCGTACG GGCTAGCTACAACGA CTCGGGA	14809
4390	CCGGAGGC G UAGCGGUG	6061	CACCGCTA GGCTAGCTACAACGA GCCTCCGG	14810
4387	GAGGCGUA G CGGUGGCG	6062	CGCCACCG GGCTAGCTACAACGA TACCGCTC	14811
4384	GCGUAGCG G UGGCGAGC	6063	GCTCGCCA GGCTAGCTACAACGA CGCTACGC	14812
4381	UAGCGGUG G CGAGCACG	6064	CGTGCTCG GGCTAGCTACAACGA CACCGCTA	14813
4377	GGUGGCGA G CACGACGA	6065	TCGTCTGT GGCTAGCTACAACGA TCGCCACC	14814
4375	UGGCGAGC A CGAGCAGC	6066	GCTCGTCG GGCTAGCTACAACGA GCTCGCCA	14815
4372	CGAGCACG A CGAGCCGC	6067	GCGGCTCG GGCTAGCTACAACGA CGTGCTCG	14816
4368	CACGACGA G CCGCGCUC	6068	GAGCGCGG GGCTAGCTACAACGA TCGTCTGT	14817
4365	GACGAGCC G CGCUCCAG	6069	CTGGAGCG GGCTAGCTACAACGA GGCTCGTC	14818
4363	CGAGCCGC G CUCCAGCC	6070	GGCTGGAG GGCTAGCTACAACGA GCGGCTCG	14819
4357	GCGCUCCA G CCGUCUCC	6071	GGAGACGG GGCTAGCTACAACGA TGGAGCGC	14820
4354	CUCCAGCC G UCUCGCU	6072	AGCGGAGA GGCTAGCTACAACGA GGCTGGAG	14821
4348	CCGUCUCC G CUUGGUCC	6073	GGACCAAG GGCTAGCTACAACGA GGAGACGG	14822
4343	UCCGCUUG G UCCAGGAC	6074	GTCCTGGA GGCTAGCTACAACGA CAAGCGGA	14823
4336	GGUCAGG A CUGUGCCG	6075	CGGCACAG GGCTAGCTACAACGA CCTGGACC	14824
4333	CCAGGACU G UGCCGAUG	6076	CATCGGCA GGCTAGCTACAACGA AGTCTTGG	14825
4331	AGGACUGU G CCGAUGCC	6077	GGCATCGG GGCTAGCTACAACGA ACAGTCTT	14826
4327	CUGUGCCG A UGCCCCAA	6078	TTTGGGCA GGCTAGCTACAACGA CGGCACAG	14827
4325	GUGCCGAU G CCCAAAUA	6079	ATTTTGGG GGCTAGCTACAACGA ATCGGCAC	14828
4318	UGCCCCAA A UGGAAGUC	6080	GACTTCCA GGCTAGCTACAACGA TTTGGGCA	14829
4312	AAAUGGAA G UCGAGUCA	6081	TGACTCGA GGCTAGCTACAACGA TTCCATTT	14830
4307	GAAGUCGA G UCAAUUGA	6082	TCAATTGA GGCTAGCTACAACGA TCGACTTC	14831
4303	UCGAGUCA A UUGAGUGG	6083	CCACTCAA GGCTAGCTACAACGA TGACTCGA	14832
4298	UCAAUUGA G UGGCACUC	6084	GAGTGCCA GGCTAGCTACAACGA TCAATTGA	14833
4295	AUUGAGUG G CACUCAUC	6085	GATGAGTG GGCTAGCTACAACGA CACTCAAT	14834
4293	UGAGUGGC A CUCAUCAC	6086	GTGATGAG GGCTAGCTACAACGA GCGACTCA	14835
4289	UGGCACUC A UCACACAU	6087	ATGTGTGA GGCTAGCTACAACGA GAGTGCCA	14836
4286	CACUCAUC A CACAUUAU	6088	ATAATGTG GGCTAGCTACAACGA GATGAGTG	14837
4284	CUCAUCAC A CAUUAUGA	6089	TCATAATG GGCTAGCTACAACGA GTGATGAG	14838
4282	CAUCACAC A UUAUGAUG	6090	CATCATAA GGCTAGCTACAACGA GTGTGATG	14839
4279	CACACAUU A UGAUGUCA	6091	TGACATCA GGCTAGCTACAACGA AATGTGTG	14840
4276	ACAUUAUG A UGUCAUAG	6092	CTATGACA GGCTAGCTACAACGA CATAATGT	14841
4274	AUUAUGAU G UCAUAGGC	6093	GCCTATGA GGCTAGCTACAACGA ATCATAAT	14842
4271	AUGAUGUC A UAGGCGCC	6094	GGCGCCTA GGCTAGCTACAACGA GACATCAT	14843
4267	UGUCAUAG G CGCCCCCA	6095	TGGGGGCG GGCTAGCTACAACGA CTATGACA	14844
4265	UCAUAGGC G CCCCCAGA	6096	TCTGGGGG GGCTAGCTACAACGA GCCTATGA	14845
4256	CCCCCAGA G CAACCACC	6097	GGTGGTTG GGCTAGCTACAACGA TCTGGGGG	14846

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4250	GAGCAACC A CCGUCGGC	6099	GCCGACGG GGCTAGCTACAACGA GGTGCTC	14848
4247	CAACCACC G UCGGCAAG	6100	CTTGCCGA GGCTAGCTACAACGA GGTGGTTG	14849
4243	CACCGUCG G CAAGGAAC	6101	GTTCTTGG GGCTAGCTACAACGA CGACGGTG	14850
4236	GGCAAGGA A CUUGCCAU	6102	ATGGCAAG GGCTAGCTACAACGA TCCTTGCC	14851
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4225	UGCCAUAG G UGGAGUAC	6105	GTACTCCA GGCTAGCTACAACGA CTATGGCA	14854
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4218	GGUGGAGU A CGUGAUGG	6107	CCATCACG GGCTAGCTACAACGA ACTCCACC	14856
4216	UGGAGUAC G UGAUGGGG	6108	CCCCATCA GGCTAGCTACAACGA GTACTCCA	14857
4213	AGUACGUG A UGGGGGCG	6109	CGCCCCCA GGCTAGCTACAACGA CACGTACT	14858
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4205	AUGGGGGC G CCCGUGGU	6111	ACCACGGG GGCTAGCTACAACGA GCCCCAT	14860
4201	GGGCGCCC G UGGUGAUG	6112	CATCACCA GGCTAGCTACAACGA GGGCGCCC	14861
4198	CGCCCGUG G UGAUGGUC	6113	GACCATCA GGCTAGCTACAACGA CACGGGCG	14862
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4186	UGGUCCUU A CCCAGUU	6116	AACTGGGG GGCTAGCTACAACGA AAGGACCA	14865
4180	UUACCCCA G UUCUGAUG	6117	CATCAGAA GGCTAGCTACAACGA TGGGGTAA	14866
4174	CAGUUCUG A UGUUAGGA	6118	TCCTAACA GGCTAGCTACAACGA CAGAAGTG	14867
4172	GUUCUGAU G UUAGGAUC	6119	GATCCTAA GGCTAGCTACAACGA ATCAGAAC	14868
4166	AUGUUAGG A UCGACACC	6120	GGTGTGCA GGCTAGCTACAACGA CCTAACAT	14869
4162	UAGGAUCG A CACCGUGU	6121	ACACGGTG GGCTAGCTACAACGA CGATCCTA	14870
4160	GGAUCGAC A CCGUGUGC	6122	GCACACGG GGCTAGCTACAACGA GTCGATCC	14871
4157	UCGACACC G UGUGCCUU	6123	AAGGCACA GGCTAGCTACAACGA GGTGTGCA	14872
4155	GACACCGU G UGCCUUAG	6124	CTAAGGCA GGCTAGCTACAACGA ACGGTGTC	14873
4153	CACCGUGU G CCUUAGAC	6125	GTCTAAGG GGCTAGCTACAACGA ACACGGTG	14874
4146	UGCCUUAG A CAUAUACG	6126	CGTATATG GGCTAGCTACAACGA CTAAGGCA	14875
4144	CCUUAGAC A UAUACGCC	6127	GGCGTATA GGCTAGCTACAACGA GTCTAAGG	14876
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4138	ACAUUAUAC G CCCAAAC	6130	GTTTGGGG GGCTAGCTACAACGA GTATATGT	14879
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4120	CUAAGGUG G CGGUAACG	6133	CGTTACCG GGCTAGCTACAACGA CACCTTAG	14882
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4088	AGCACUUU G UACCCUUG	6141	CAAGGGTA GGCTAGCTACAACGA AAAGTGCT	14890
4086	CACUUUGU A CCCUUGGG	6142	CCCAAGGG GGCTAGCTACAACGA ACAAAGTG	14891
4078	ACCCUUGG G CUGCAUUA	6143	ATATGCAG GGCTAGCTACAACGA CCAAGGGT	14892
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4069	CUGCAUUA G CAGCCGGU	6147	ACCGGCTG GGCTAGCTACAACGA ATATGCAG	14896
4066	CAUAUGCA G CCGGUACC	6148	GGTACCGG GGCTAGCTACAACGA TGCATATG	14897
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4060	CAGCCGGU A CCUUAGUG	6150	CACTAAGG GGCTAGCTACAACGA ACCGGCTG	14899
4054	GUACCUUA G UGCUCUUG	6151	CAAGAGCA GGCTAGCTACAACGA TAAGGTAC	14900
4052	ACCUUAGU G CUCUUGCC	6152	GGCAAGAG GGCTAGCTACAACGA ACTAAGGT	14901
4046	GUGCUCUU G CCGUGGCC	6153	GGCAGCGG GGCTAGCTACAACGA AAGAGCAC	14902

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4028	GUGGGAGC G UGUAGGUG	6158	CACCTACA GGCTAGCTACAACGA GCTCCAC	14907
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4022	GCGUGUAG G UGGGCCAC	6160	GTGGCCCA GGCTAGCTACAACGA CTACACGC	14909
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3980	GGGGACGA G UUGCCGU	6170	ACGGACAA GGCTAGCTACAACGA TCGTCCCC	14919
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3967	CCGUGAAG A CCGGGGAC	6173	GTCCCCGG GGCTAGCTACAACGA CTTACGG	14922
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3957	CGGGGACC G CAUGGUAG	6175	CTACCATG GGCTAGCTACAACGA GGTCCCCG	14924
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3952	ACCGCAUG G UAGUUUCC	6177	GGAACTA GGCTAGCTACAACGA CATGCGGT	14926
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3896	CCCCGGGU G CACACAGC	6190	GCTGTGTG GGCTAGCTACAACGA ACCGGGGG	14939
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3785	CUCCCCU G CUGUCACC	6213	GGTGACAG GGCTAGCTACAACGA AGGGGGAG	14962
3782	CCCCUGCU G UCACCCCG	6214	CGGGGTGA GGCTAGCTACAACGA AGCAGGGG	14963
3779	CUGCUGUC A CCCCGCCG	6215	CGGCGGGG GGCTAGCTACAACGA GACAGCAG	14964
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3710	CCGCAGGU G CAUGGUGU	6234	ACACCATG GGCTAGCTACAACGA ACCTGCGG	14983
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3575	ACAGUCCA G CACACGCC	6267	GGCGTGTG GGCTAGCTACAACGA TGGACTGT	15016
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3553	CGCAGGUC G CUAGGAAA	6275	TTTCCTAG GGCTAGCTACAACGA GACCTGCG	15024
3543	UAGGAAAG A CUGCGUCG	6276	CGACGCAG GGCTAGCTACAACGA CTTTCCTA	15025
3540	GAAAGACU G CGUCGCGG	6277	CCGCGACG GGCTAGCTACAACGA AGTCTTTC	15026
3538	AAGACUGC G UCGCGGUG	6278	CACCGCGA GGCTAGCTACAACGA GCAGTCTT	15027
3535	ACUGCGUC G CGGUGGAA	6279	TTCCACCG GGCTAGCTACAACGA GACGCAGT	15028
3532	GCGUCGCG G UGGAAACC	6280	GGTTTCCA GGCTAGCTACAACGA CGCGACGC	15029
3526	CGGUGGAA A CCACUUGA	6281	TCAAGTGG GGCTAGCTACAACGA TTCCACCG	15030
3523	UGGAAACC A CUUGAACU	6282	AGTTCAAG GGCTAGCTACAACGA GGTTTCCA	15031
3517	CCACUUGA A CUUCCCC	6283	GGGGGAAG GGCTAGCTACAACGA TCAAGTGG	15032
3505	CCCCUCG A CUUGGUUC	6284	GAACCAAG GGCTAGCTACAACGA CGAGGGGG	15033
3500	UCGACUUG G UUCUUGUC	6285	GACAAGAA GGCTAGCTACAACGA CAAGTCGA	15034
3494	UGGUUCUU G UCCCGGCC	6286	GGCCGGGA GGCTAGCTACAACGA AAGAACCA	15035
3488	UUGUCCCG G CCCGUGAG	6287	CTCACGGG GGCTAGCTACAACGA CGGGACAA	15036
3484	CCCGGCC G UGAGGCUG	6288	CAGCCTCA GGCTAGCTACAACGA GGGCCGGG	15037
3479	CCCGUGAG G CUGGUGAU	6289	ATCACCAG GGCTAGCTACAACGA CTCACGGG	15038
3475	UGAGGCUG G UGAUAAUG	6290	CATTATCA GGCTAGCTACAACGA CAGCCTCA	15039
3472	GGCUGGUG A UAAUGCAG	6291	CTGCATTA GGCTAGCTACAACGA CACCAGCC	15040
3469	UGGUGAUA A UGCAGCCA	6292	TGGCTGCA GGCTAGCTACAACGA TATCACCA	15041
3467	GUGAUAAU G CAGCCAAA	6293	TTTGGCTG GGCTAGCTACAACGA ATTATCAC	15042
3464	AUAAUGCA G CCAAACAG	6294	CTGTTTGG GGCTAGCTACAACGA TGCATTAT	15043
3459	GCAGCCAA A CAGGCCCC	6295	GGGGCCTG GGCTAGCTACAACGA TTGGCTGC	15044
3455	CCAAACAG G CCCCGCGU	6296	ACGCGGGG GGCTAGCTACAACGA CTGTTTGG	15045
3450	CAGGCCCC G CGUCUGUU	6297	AACAGACG GGCTAGCTACAACGA GGGGCCTG	15046
3448	GGCCCCG G UCUGUUGG	6298	CCAACAGA GGCTAGCTACAACGA GCGGGGCC	15047
3444	CCGCGUCU G UUGGGAGU	6299	ACTCCCAA GGCTAGCTACAACGA AGACGCGG	15048
3437	UGUUGGGA G UAGGCCGU	6300	ACGGCCTA GGCTAGCTACAACGA TCCCAACA	15049
3433	GGGAGUAG G CCGUAAUG	6301	CATTACGG GGCTAGCTACAACGA CTACTCCC	15050
3430	AGUAGGCC G UAAUGGCG	6302	GCCCATTA GGCTAGCTACAACGA GGCCTACT	15051
3427	AGGCCGUA A UGGGCGCG	6303	CGCGCCCA GGCTAGCTACAACGA TACGGCCT	15052
3423	CGUAAUGG G CGCGAGGA	6304	TCCTCGCG GGCTAGCTACAACGA CCATTACG	15053
3421	UAAUGGGC G CGAGGAGU	6305	ACTCCTCG GGCTAGCTACAACGA GCCCATTA	15054
3414	CGCGAGGA G UCGCCACC	6306	GGTGGCGA GGCTAGCTACAACGA TCCTCGCG	15055
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3389	UCAAGACU G UCGGUCGG	6311	CCAGCCGA GGCTAGCTACAACGA AGTCTTGA	15060
3385	GACUGUCG G CUGGUCCU	6312	AGGACCAG GGCTAGCTACAACGA CGACAGTC	15061
3381	GUCGGCUG G UCCUAGGA	6313	TCCTAGGA GGCTAGCTACAACGA CAGCCGAC	15062
3372	UCCUAGGA G UAUCUCCC	6314	GGGAGATA GGCTAGCTACAACGA TCCTAGGA	15063
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3352	CCCUUCGG G CGGAGACA	6316	TGTCFCCG GGCTAGCTACAACGA CCGAAGGG	15065
3346	GGGCGGAG A CAGGUAGA	6317	TCTACTTG GGCTAGCTACAACGA CTCCGCC	15066
3342	GGAGACAG G UAGACCCA	6318	TGGGTCTA GGCTAGCTACAACGA CTGTCTCC	15067
3338	ACAGGUAG A CCCAUAAU	6319	ATTATGGG GGCTAGCTACAACGA CTACTGT	15068
3334	GUAGACCC A UAAUGAUG	6320	CATCATTA GGCTAGCTACAACGA GGGTCTAC	15069
3331	GACCCAU A UGAUGUCC	6321	GGACATCA GGCTAGCTACAACGA TATGGGTC	15070

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3326	AUAAUGAU G UCCCCACA	6323	TGTGGGGA GGCTAGCTACAACGA ATCATTAT	15072
3320	AUGUCCCC A CACGCCGC	6324	GCGGCGTG GGCTAGCTACAACGA GGGGACAT	15073
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3316	CCCCACAC G CCGCGGUG	6326	CACCGCGG GGCTAGCTACAACGA GTGTGGGG	15075
3313	CACACGCC G CGGUGUCU	6327	AGACACCG GGCTAGCTACAACGA GCGTGTGT	15076
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3292	CCCAGGUG A UGAUCUUG	6331	CAAGATCA GGCTAGCTACAACGA CACCTGGG	15080
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3277	UGAUUUC A UGUCGGAG	6334	CTCCGACA GGCTAGCTACAACGA GGAAATCA	15083
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3244	CCGCUACC G CAGGUCU	6342	AGACCTGG GGCTAGCTACAACGA GGTAGCGG	15091
3239	ACCGCCAG G UCUCGUAG	6343	CTACGAGA GGCTAGCTACAACGA CTGGCGGT	15092
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3220	CUGUGUGG G CCCAGUCC	6348	GGACTGGG GGCTAGCTACAACGA CCACACAG	15097
3215	UGGGCCCA G UCCUGCAG	6349	CTGCAGGA GGCTAGCTACAACGA TGGGCCCA	15098
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3194	GUGAGGUG G UCAUAGAC	6354	GTCTATGA GGCTAGCTACAACGA CACCTCAC	15103
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3181	AGACGGAC G UACCUUUC	6358	GAAAGGTA GGCTAGCTACAACGA GTCCGTCT	15107
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3166	UCAAUUCG G CCAACUUC	6361	GAAGTTGG GGCTAGCTACAACGA CGAATTGA	15110
3162	UUCGCCCA A CUUCAUGA	6362	TCATGAAG GGCTAGCTACAACGA TGGCCGAA	15111
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3135	GACAUUUU G CCCCCAC	6369	GTGGGGGG GGCTAGCTACAACGA AATATGTC	15118
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3079	GAGCCCGC A CAAAGUCC	6382	GGACTTTG GGCTAGCTACAACGA GCGGGCTC	15131
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3013	CGAGCAUA A UUUUGGUG	6400	CACCAAAA GGCTAGCTACAACGA TATGCTCG	15149
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2956	GAAUGAUG G CACCGCGC	6414	GCGCGGTG GGCTAGCTACAACGA CATCATTC	15163
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2917	GGAUCCAC A CUUGCAAC	6422	GTTGCAAG GGCTAGCTACAACGA GTGGATCC	15171
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2905	GCAACUGC G CCUCGGCU	6426	AGCCGAGG GGCTAGCTACAACGA GCAGTTGC	15175
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2893	CGGCUCUG G UGAUAAGG	6428	CCTTATCA GGCTAGCTACAACGA CAGAGCCG	15177
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2883	GAUAAGGU A UUGCAACC	6431	GGTTGCAA GGCTAGCTACAACGA ACCTTATC	15180
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2746	GUGGUAAC G CCAGCAGG	6470	CCTGCTGG GGCTAGCTACAACGA GTTACCAC	15219
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2727	CAGGAGUA G CGGCCAUA	6474	TATGGCCG GGCTAGCTACAACGA TACTCCTG	15223
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2626	UGCCAUGC A CUCCGGCC	6500	GGCCGGAG GGCTAGCTACAACGA GCATGGCA	15249
2620	GCACUCCG G CCAAGGAU	6501	ATCCTTGG GGCTAGCTACAACGA CGGAGTGC	15250
2613	GGCCAAGG A UGCUGCAU	6502	ATGCAGCA GGCTAGCTACAACGA CCTTGGCC	15251
2611	CCAAGGAU G CUGCAUUG	6503	CAATGCAG GGCTAGCTACAACGA ATCCTTGG	15252
2608	AGGAUGCU G CAUUGAGG	6504	CCTCAATG GGCTAGCTACAACGA AGCATCCT	15253
2606	GAUGCUGC A UUGAGGAC	6505	GTCCTCAA GGCTAGCTACAACGA GCAGCATC	15254
2599	CAUUGAGG A CCACCAGG	6506	CCTGGTGG GGCTAGCTACAACGA CCTCAATG	15255
2596	UGAGGACC A CCGGUUC	6507	GAACCTGG GGCTAGCTACAACGA GGTCTCTA	15256
2591	ACCACCAG G UUCUCUAG	6508	CTAGAGAA GGCTAGCTACAACGA CTGGTGGT	15257
2581	UCUCUAGG G CAGCCUCG	6509	CGAGGCTG GGCTAGCTACAACGA CCTAGAGA	15258
2578	CUAGGGCA G CCUCGGCC	6510	GGCCGAGG GGCTAGCTACAACGA TGCCCTAG	15259
2572	CAGCCUCG G CCUGGGCU	6511	AGCCGAGG GGCTAGCTACAACGA CGAGGCTG	15260
2566	CGGCCUGG G CUACCAAC	6512	GTTGGTAG GGCTAGCTACAACGA CCAGGCCG	15261
2563	CCUGGGCU A CCAACAGC	6513	GCTGTTGG GGCTAGCTACAACGA AGCCGAGG	15262
2559	GGCUACCA A CAGCAUCA	6514	TGATGCTG GGCTAGCTACAACGA TGGTAGCC	15263
2556	UACCAACA G CAUCAUCC	6515	GGATGATG GGCTAGCTACAACGA TGTGGTGA	15264
2554	CCAACAGC A UCAUCCAC	6516	GTGGATGA GGCTAGCTACAACGA GCTGTTGG	15265
2551	ACAGCAUC A UCCACAAA	6517	TTGTGTTG GGCTAGCTACAACGA GATGCTGT	15266
2547	CAUCAUCC A CAAACAGG	6518	CCTGTTTG GGCTAGCTACAACGA GGATGATG	15267
2543	AUCCACAA A CAGGCACA	6519	TGTGCCTG GGCTAGCTACAACGA TTGTGGAT	15268
2539	ACAAACAG G CACAGACG	6520	CGTCTGTG GGCTAGCTACAACGA CTGTTTGT	15269
2537	AAACAGGC A CAGACGCG	6521	CGCGTCTG GGCTAGCTACAACGA GCCTGTTT	15270
2533	AGGCACAG A CGCGCGCG	6522	CGCGCGCG GGCTAGCTACAACGA CTGTGCCT	15271
2531	GCACAGAC G CGCGCGUC	6523	GACGCGCG GGCTAGCTACAACGA GTCTGTGC	15272
2529	ACAGACGC G CGCGUCUG	6524	CAGACGCG GGCTAGCTACAACGA GCGTCTGT	15273
2527	AGACGCGC G CGUCUGCC	6525	GGCAGACG GGCTAGCTACAACGA GCGGCTCT	15274
2525	ACGCGCGC G UCUGCCAG	6526	CTGGCAGA GGCTAGCTACAACGA GCGGCGCT	15275
2521	GCGCGUCU G CCAGGAGA	6527	TCTCCTGG GGCTAGCTACAACGA AGACGCGC	15276
2505	AAGGAAAA G CAACAGGA	6528	TCCTGTTG GGCTAGCTACAACGA TTTTCCTT	15277
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2497	GCAACAGG A CAUACUCC	6530	GGAGTATG GGCTAGCTACAACGA CCTGTTGC	15279
2495	AACAGGAC A UACUCCCA	6531	TGGGAGTA GGCTAGCTACAACGA GTCCTGTT	15280
2493	CAGGACAU A CUCCCAUU	6532	AATGGGAG GGCTAGCTACAACGA ATGTCCTG	15281
2487	AUACUCCC A UUUGAUUG	6533	CAATCAAA GGCTAGCTACAACGA GGGAGTAT	15282
2482	CCCAUUUG A UUGCGAAG	6534	CTTCGCAA GGCTAGCTACAACGA CAAATGGG	15283
2479	AUUUGAUU G CGAAGGAG	6535	CTCCTTCG GGCTAGCTACAACGA AATCAAT	15284
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2467	AGGAGACA A CCGCUGAC	6537	GTCAGCGG GGCTAGCTACAACGA TGTCTCCT	15286
2464	AGACAACC G CUGACCCU	6538	AGGGTCAG GGCTAGCTACAACGA GGTGTCTT	15287
2460	AACCGCUG A CCCUACAC	6539	GTGTAGGG GGCTAGCTACAACGA CAGCGGTT	15288
2455	CUGACCCU A CACCGUAC	6540	GTACGGTG GGCTAGCTACAACGA AGGGTCAG	15289
2453	GACCCUAC A CCGUACAG	6541	CTGTACGG GGCTAGCTACAACGA GTAGGTCT	15290
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2444	CCGUACAG G UAUUGCAC	6544	GTGCAATA GGCTAGCTACAACGA CTGTACGG	15293
2442	GUACAGGU A UUGCACGU	6545	ACGTGCAA GGCTAGCTACAACGA ACCTGTAC	15294

2439	CAGGUUUU G CACGUCCA	6546	TGGACGTG GGCTAGCTACAACGA AATACCTG	15295
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2435	UAUUGCAC G UCCACGAU	6548	ATCGTGGA GGCTAGCTACAACGA GTGCAATA	15297
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2428	CGUCCACG A UGUUCUGG	6550	CCAGAACA GGCTAGCTACAACGA CGTGGACG	15299
2426	UCCACGAU G UUCUGGUG	6551	CACCAGAA GGCTAGCTACAACGA ATCGTGGA	15300
2420	AUGUUCUG G UGGAGAUG	6552	CATCTCCA GGCTAGCTACAACGA CAGAACAT	15301
2414	UGGUGGAG A UGGAUCAA	6553	TTGATCCA GGCTAGCTACAACGA CTCCACCA	15302
2410	GGAGAUGG A UCAAACCA	6554	TGGTTTGA GGCTAGCTACAACGA CCACTCTCC	15303
2405	UGGAUCAA A CCAGUGGA	6555	TCCACTGG GGCTAGCTACAACGA TTGATCCA	15304
2401	UCAAACCA G UGGACAGA	6556	TCTGTCCA GGCTAGCTACAACGA TGGTTTGA	15305
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2392	UGGACAGA G CCGGUAGG	6558	CCTACCGG GGCTAGCTACAACGA TCTGTCCA	15307
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2383	CCGGUAGG G UGUGAAG	6560	CTTCACCA GGCTAGCTACAACGA CCTACCGG	15309
2380	GUAGGGUG G UGAAGGAG	6561	CTCCTTCA GGCTAGCTACAACGA CACCTTAC	15310
2372	GUGAAGGA G CAGGGCAG	6562	CTGCCCTG GGCTAGCTACAACGA TCCTTCAC	15311
2367	GGAGCAGG G CAGUUAUU	6563	AAATACTG GGCTAGCTACAACGA CCTCTCC	15312
2364	GCAGGGCA G UAUUUGCC	6564	GGCAAATA GGCTAGCTACAACGA TGCCCTGC	15313
2362	AGGGCAGU A UUUGCCAC	6565	GTGGCAAA GGCTAGCTACAACGA ACTGCCCT	15314
2358	CAGUAUUU G CCACUCUG	6566	CAGAGTGG GGCTAGCTACAACGA AAATACTG	15315
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2350	GCCACUCU G UAGUGGAC	6568	GTCCACTA GGCTAGCTACAACGA AGAGTGGC	15317
2347	ACUCUGUA G UGACAAC	6569	GTGTGTCCA GGCTAGCTACAACGA TACAGAGT	15318
2343	UGUAGUGG A CAACAGCA	6570	TGCTGTTG GGCTAGCTACAACGA CCACTACA	15319
2340	AGUGGACA A CAGCAGCG	6571	CGCTGCTG GGCTAGCTACAACGA TGTCCACT	15320
2337	GGACAACA G CAGCGGGC	6572	GCCCCGTG GGCTAGCTACAACGA TGTGTGCC	15321
2334	CAACAGCA G CGGGCUGA	6573	TCAGCCCG GGCTAGCTACAACGA TGCTGTTG	15322
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2325	CGGGCUGA G CUCUGAUC	6575	GATCAGAG GGCTAGCTACAACGA TCAGCCCG	15324
2319	GAGCUCUG A UCUGUCCC	6576	GGGACAGA GGCTAGCTACAACGA CAGAGCTC	15325
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2300	UCCUCCAA A UCACAACG	6579	CGTTGTGA GGCTAGCTACAACGA TTGGAGGA	15328
2297	UCCAAUUC A CAACGCUC	6580	GAGCGTTG GGCTAGCTACAACGA GATTGTGA	15329
2294	AAAUCACA A CGCUCUCC	6581	GGAGAGCG GGCTAGCTACAACGA TGTGATTT	15330
2292	AUCACAAC G CUCUCCUC	6582	GAGGAGAG GGCTAGCTACAACGA GTTGTGAT	15331
2281	CUCCUCGA G UCCAAUUG	6583	CAATTGGA GGCTAGCTACAACGA TCGAGGAG	15332
2276	CGAGUCCA A UUGCAUGC	6584	GCATGCAA GGCTAGCTACAACGA TGGACTCG	15333
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2271	CCAAUUGC A UGCGCGG	6586	CCGCCGCA GGCTAGCTACAACGA GCAATTGG	15335
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2266	UGCAUGCG G CGGUGAGC	6588	GCTCACCG GGCTAGCTACAACGA CGCATGCA	15337
2263	AUGCGGCG G UGAGCCUG	6589	CAGGCTCA GGCTAGCTACAACGA CGCCGCAT	15338
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2253	GAGCCUGU G CUCCACGC	6592	GCGTGGAG GGCTAGCTACAACGA ACAGGCTC	15341
2248	UGUGCUCC A CGCCCCC	6593	GGGGGGCG GGCTAGCTACAACGA GGAGCACA	15342
2246	UGCUCAC G CCCCCAC	6594	GTGGGGGG GGCTAGCTACAACGA GTGGAGCA	15343
2239	CGCCCCC A CAUACAUC	6595	GATGTATG GGCTAGCTACAACGA GGGGGGCG	15344
2237	CCCCCAC A UACAUCU	6596	AGGATGTA GGCTAGCTACAACGA GTGGGGGG	15345
2235	CCCCACAU A CAUCCUAA	6597	TTAGGATG GGCTAGCTACAACGA ATGTGGGG	15346
2233	CCACAUC A UCCUAACC	6598	GGTTAGGA GGCTAGCTACAACGA GTATGTGG	15347
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2218	CCUUAAG A UGAAAAA	6600	TTTTTCCA GGCTAGCTACAACGA CTTTAAGG	15349
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2167	GGUAGUCA A CUAUGCAU	6613	ATGCATAG GGCTAGCTACAACGA TGACTACC	15362
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2160	AACUAUGC A UCUAGGUG	6616	CACCTAGA GGCTAGCTACAACGA GCATAGTT	15365
2154	GCAUCUAG G UGUUAACC	6617	GGTTAACA GGCTAGCTACAACGA CTAGATGC	15366
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2123	CACUUUGC G UAAGUGGC	6625	GCCACTTA GGCTAGCTACAACGA GCAAAGTG	15374
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2116	CGUAAGUG G CCUCGGGG	6627	CCCCGAGG GGCTAGCTACAACGA CACTTACG	15376
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2106	CUCGGGGU G CUUCCGGA	6629	TCCGGAAG GGCTAGCTACAACGA ACCCGAG	15378
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2089	AGCAGUCC G UGGGGCAG	6632	CTGCCCA GGCTAGCTACAACGA GGACTGCT	15381
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2053	CCCCCCCG A UGUUGCAC	6640	GTGCAACA GGCTAGCTACAACGA CGGGGGGG	15389
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2048	CCGAUGUU G CACGGGGG	6642	CCCCCGTG GGCTAGCTACAACGA AACATCGG	15391
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2039	CACGGGGG G CCCCCGCA	6644	TGCGGGGG GGCTAGCTACAACGA CCCCCTGT	15393
2033	GGGCCCCC G CACGUCUU	6645	AAGACGTG GGCTAGCTACAACGA GGGGGCCC	15394
2031	GCCCCCGC A CGUCUUGG	6646	CCAAGACG GGCTAGCTACAACGA GCGGGGGC	15395
2029	CCCCGCAC G UCUUGGUG	6647	CACCAAGA GGCTAGCTACAACGA GTGCGGGG	15396
2023	ACGUCUUG G UGAACCCA	6648	TGGGTTCA GGCTAGCTACAACGA CAAGACGT	15397
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2012	AACCCAGU G CCAUUCAU	6651	ATGAATGG GGCTAGCTACAACGA ACTGGGTT	15400
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2005	UGCAUUC A UCCAUGUG	6653	CACATGGA GGCTAGCTACAACGA GAATGGCA	15402
2001	AUCAUCC A UGUGCAGC	6654	GCTGCACA GGCTAGCTACAACGA GGATGAAT	15403
1999	UCAUCCAU G UGCAGCCG	6655	CGGCTGCA GGCTAGCTACAACGA ATGGATGA	15404
1997	AUCCAUGU G CAGCCGAA	6656	TTCGGCTG GGCTAGCTACAACGA ACATGGAT	15405
1994	CAUGUGCA G CCGAACCA	6657	TGGTTCGG GGCTAGCTACAACGA TGCACATG	15406

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1985	CCGAACCA G UUGCCUUG	6659	CAAGGCAA GGCTAGCTACAACGA TGGTTCGG	15408
1982	AACCAGUU G CCUUGCGG	6660	CCGCAAGG GGCTAGCTACAACGA AACTGGTT	15409
1977	GUUGCCUU G CGGCGGCC	6661	GGCCGCCG GGCTAGCTACAACGA AAGGCAAC	15410
1974	GCCUUGCG G CGGCCGCG	6662	CGCGGCCG GGCTAGCTACAACGA CGCAAGGC	15411
1971	UUGCGGCG G CCGCGUGU	6663	ACACGCGG GGCTAGCTACAACGA CGCCGCAA	15412
1968	CGGCGGCC G CGUGUUGU	6664	ACAACACG GGCTAGCTACAACGA GGCCGCCG	15413
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1950	GAGGAGCA G CAGUCCG	6669	CGGACGTG GGCTAGCTACAACGA TGCTCCTC	15418
1948	GGAGCAGC A CGUCCGUC	6670	GACGGACG GGCTAGCTACAACGA GCTGCTCC	15419
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1942	GCACGUCC G UCUCGUUC	6672	GAACGAGA GGCTAGCTACAACGA GGACGTGC	15421
1937	UCCGUCUC G UUCGCCCC	6673	GGGGCGAA GGCTAGCTACAACGA GAGACGGA	15422
1933	UCUCGUUC G CCCCCAG	6674	CTGGGGGG GGCTAGCTACAACGA GAACGAGA	15423
1925	GCCCCCA G UUAUACGU	6675	ACGTATAA GGCTAGCTACAACGA TGGGGGGC	15424
1922	CCCCAGUU A UACUGGG	6676	CCCAGTGA GGCTAGCTACAACGA AACTGGGG	15425
1920	CCAGUUAU A CUGUGGGG	6677	CCCCCAGG GGCTAGCTACAACGA ATAATGG	15426
1918	AGUUAUAC G UGGGGGCG	6678	CGCCCCCA GGCTAGCTACAACGA GTATAACT	15427
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1901	CCGAAACG G UCGGUCGU	6682	ACGACCGA GGCTAGCTACAACGA CGTTTCGG	15431
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1894	GGUCGGUC G UCCCCACC	6684	GGTGGGGA GGCTAGCTACAACGA GACCGACC	15433
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1885	UCCCCACC A CAACAGGG	6686	CCCTGTGG GGCTAGCTACAACGA GGTGGGGA	15435
1882	CCACCACA A CAGGGCUU	6687	AAGCCCTG GGCTAGCTACAACGA TGTGGTGG	15436
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1865	GGGGUGAA G CAUACAC	6690	GTGTATTG GGCTAGCTACAACGA TTCACCCC	15439
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1853	UACACUGG A CCACAUAC	6694	GTATGTGG GGCTAGCTACAACGA CCAGTGTA	15443
1850	ACUGGACC A CAUACCUG	6695	CAGGTATG GGCTAGCTACAACGA GGTCCAGT	15444
1848	UGGACCAC A UACCUGCG	6696	CGCAGGTA GGCTAGCTACAACGA GTGGTCCA	15445
1846	GACCACAU A CCUGCGAU	6697	ATCGCAGG GGCTAGCTACAACGA ATGTGGTC	15446
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1833	CGAUGCGG G UACGAUAC	6701	GTATCGTA GGCTAGCTACAACGA CCGCATCG	15450
1831	AUGCGGGU A CGAUACCA	6702	TGGTATCG GGCTAGCTACAACGA ACCCGCAT	15451
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1826	GGUACGAU A CCACACGG	6704	CCGTGTGG GGCTAGCTACAACGA ATCGTACC	15453
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1821	GAUACCAC A CGGCCGCG	6706	CGCGGCCG GGCTAGCTACAACGA GTGGTATC	15455
1818	ACCACACG G CCGCGGUG	6707	CACCGCGG GGCTAGCTACAACGA CGTGTGGT	15456
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1805	GGUGCGUA G UGCCAGCA	6712	TGCTGGCA GGCTAGCTACAACGA TACGCACC	15461
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1796	UGCCAGCA A UAGGGCCU	6715	AGGCCCTA GGCTAGCTACAACGA TGCTGGCA	15464
1791	GCAAUAGG G CCUCUGGU	6716	ACCAGAGG GGCTAGCTACAACGA CCTATTGC	15465
1784	GGCCUCUG G UCCGAGUU	6717	AACTCGGA GGCTAGCTACAACGA CAGAGGCC	15466
1778	UGGUCCGA G UUGUGGCC	6718	GGCCACAA GGCTAGCTACAACGA TCGGACCA	15467
1775	UCCGAGUU G UGGCCUC	6719	GAGGGCCA GGCTAGCTACAACGA AACTCGGA	15468
1772	GAGUUGUG G CCCUCGU	6720	ACCGAGGG GGCTAGCTACAACGA CACAACCTC	15469
1765	GGCCUCUG G UGUAGGUG	6721	CACCTACA GGCTAGCTACAACGA CGAGGGCC	15470
1763	CCCUCGU G UAGGUGAU	6722	ATCACCTA GGCTAGCTACAACGA ACCGAGGG	15471
1759	CGGUGUAG G UGAUAGGA	6723	TCCTATCA GGCTAGCTACAACGA CTACACCG	15472
1756	UGUAGGUG A UAGGACCC	6724	GGGTCTTA GGCTAGCTACAACGA CACCTACA	15473
1751	GUGAUAGG A CCCACCC	6725	GGGTGGGG GGCTAGCTACAACGA CCTATCAC	15474
1746	AGGACCCC A CCCUGAG	6726	CTCAGGGG GGCTAGCTACAACGA GGGGTCTT	15475
1738	ACCCUGA G CGAACUUG	6727	CAAGTTCG GGCTAGCTACAACGA TCAGGGGT	15476
1734	CUGAGCGA A CUUGUCAA	6728	TTGACAA G GGCTAGCTACAACGA TCGTCTAG	15477
1730	GCGAACUU G UCAAUGGA	6729	TCCATTGA GGCTAGCTACAACGA AAGTTCGC	15478
1726	ACUUGUCA A UGGAGCG	6730	CCGCTCCA GGCTAGCTACAACGA TGACAAGT	15479
1721	UCAAUUGA G CGGCAGCU	6731	AGCTGCCG GGCTAGCTACAACGA TCCATTGA	15480
1718	AUGGAGCG G CAGCUGGC	6732	GCCAGCTG GGCTAGCTACAACGA CGTCCAT	15481
1715	GAGCGGCA G CUGGCCAA	6733	TTGGCCAG GGCTAGCTACAACGA TGCCGCTC	15482
1711	GGCAGCUG G CCAAGCGC	6734	GCGCTTGG GGCTAGCTACAACGA CAGCTGCC	15483
1706	CUGGCCAA G CGCUGUGG	6735	CCACAGCG GGCTAGCTACAACGA TTGGCCAG	15484
1704	GGCCAAGC G CUGUGGGC	6736	GCCCACAG GGCTAGCTACAACGA GCTTGCC	15485
1701	CAAGCGCU G UGGGCAUC	6737	GATGCCCA GGCTAGCTACAACGA AGCGCTTG	15486
1697	CGCUGUGG G CAUCCGGA	6738	TCCGATG GGCTAGCTACAACGA CCACAGCG	15487
1695	CUGUGGGC A UCCGGACG	6739	CGTCCGGA GGCTAGCTACAACGA GCCCAGAG	15488
1689	GCAUCCGG A CGAGUUGA	6740	TCAACTCG GGCTAGCTACAACGA CCGGATGC	15489
1685	CCGCACGA G UUGAACCU	6741	AGGTTCAA GGCTAGCTACAACGA TCGTCCGG	15490
1680	CGAGUUGA A CCUGUGUG	6742	CACACAGG GGCTAGCTACAACGA TCAACTCG	15491
1676	UUGAACCU G UGUGCAUA	6743	TATGCACA GGCTAGCTACAACGA AGGTTCAA	15492
1674	GAACCUGU G UGCAUAGA	6744	TCTATGCA GGCTAGCTACAACGA ACAGGTTC	15493
1672	ACCUGUGU G CAUAGAAC	6745	GTTCTATG GGCTAGCTACAACGA ACACAGGT	15494
1670	CUGUGUGC A UAGAACAG	6746	CTGTCTTA GGCTAGCTACAACGA GCACACAG	15495
1665	UGCAUAGA A CAGUGCAG	6747	CTGCACTG GGCTAGCTACAACGA TCTATGCA	15496
1662	AUAGAACA G UGCAGCAA	6748	TTGTGCA GGCTAGCTACAACGA TGTCTAT	15497
1660	AGAACAGU G CAGCAAUG	6749	CATTGCTG GGCTAGCTACAACGA ACTGTCT	15498
1657	ACAGUGCA G CAAUGAAC	6750	GTTTATTG GGCTAGCTACAACGA TGCATGT	15499
1654	GUGCAGCA A UGAACCCG	6751	CGGGTTCA GGCTAGCTACAACGA TGCTGCAC	15500
1650	AGCAAUGA A CCCGGUUU	6752	AAACCGGG GGCTAGCTACAACGA TCATTGCT	15501
1645	UGAACCCG G UUUGGAGG	6753	CCTCCAAA GGCTAGCTACAACGA CGGGTTCA	15502
1634	UGGAGGGA G UCAUUGCA	6754	TGCAATGA GGCTAGCTACAACGA TCCCTCCA	15503
1631	AGGAGAGC A UUGCAGUU	6755	AACTGCAA GGCTAGCTACAACGA GACTCCCT	15504
1628	GAGUCAUU G CAGUUCAG	6756	CTGAAGTG GGCTAGCTACAACGA AATGACTC	15505
1625	UCAUUGCA G UUCAGGGC	6757	GCCCTGAA GGCTAGCTACAACGA TGCAATGA	15506
1618	AGUUCAGG G CAGUCCUG	6758	CAGGACTG GGCTAGCTACAACGA CCTGAAGT	15507
1615	UCAGGGCA G UCCUGUUA	6759	TAACAGGA GGCTAGCTACAACGA TGCCCTGA	15508
1610	GCAGUCCU G UUAUGUG	6760	CACATTAA GGCTAGCTACAACGA AGGACTGC	15509
1606	UCCUGUUA A UGUGCCAG	6761	CTGGCACA GGCTAGCTACAACGA TAACAGGA	15510
1604	CUGUUAU G UGCCAGCU	6762	AGCTGGCA GGCTAGCTACAACGA ATTAACAG	15511
1602	GUUAUUGU G CCAGCUGC	6763	GCAGCTGG GGCTAGCTACAACGA ACATTAA	15512
1598	AUGUGCCA G CUGCCGUU	6764	AACGGCAG GGCTAGCTACAACGA TGGCACAT	15513
1595	UGCCAGCU G CCGUUGGU	6765	ACCAACGG GGCTAGCTACAACGA AGCTGGCA	15514
1592	CAGCUGCC G UUGGUGUU	6766	AACACCAA GGCTAGCTACAACGA GGCAGCTG	15515
1588	UGCCGUUG G UGUUAUA	6767	TATTAACA GGCTAGCTACAACGA CAACGGCA	15516
1586	CCGUUGGU G UUAUAAG	6768	CTTATTAA GGCTAGCTACAACGA ACCAACGG	15517
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1571	AGCUGGAU A UUCUGAGA	6772	TCTCAGAA GGCTAGCTACAACGA ATCCAGCT	15521
1563	AUUCUGAG A UGUCCAG	6773	CTGGAGCA GGCTAGCTACAACGA CTCAGAAT	15522
1561	UCUGAGAU G CUCCAGAU	6774	ATCTGGAG GGCTAGCTACAACGA ATCTCAGA	15523
1554	UGCUCAG A UGUAAAGA	6775	TCTTTACA GGCTAGCTACAACGA CTGGAGCA	15524
1552	CUCCAGAU G UAAAGAGG	6776	CCTCTTTA GGCTAGCTACAACGA ATCTGGAG	15525
1542	AAAGAGGG A UGCCACCC	6777	GGGTGGCA GGCTAGCTACAACGA CCCTCTTT	15526
1540	AGAGGGAU G CCACCCUA	6778	TAGGGTGG GGCTAGCTACAACGA ATCCCTCT	15527
1537	GGGAUGCC A CCCUACUA	6779	TAGTAGGG GGCTAGCTACAACGA GGCATCCC	15528
1532	GCCACCCU A CUAGUGGU	6780	ACCACCTAG GGCTAGCTACAACGA AGGGTGGC	15529
1528	CCCUCUA G UGGUGUGG	6781	CCACACCA GGCTAGCTACAACGA TAGTAGGG	15530
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1515	GUGGCCU G CGCCCCC	6785	GGGGGGCG GGCTAGCTACAACGA AGGGCCAC	15534
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1501	CCCUUGUC G UGUAGGUG	6788	CACCTACA GGCTAGCTACAACGA GACAGGGG	15537
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1495	UCGUGUAG G UGUCCCCG	6790	CGGGGACA GGCTAGCTACAACGA CTACACGA	15539
1493	GUGUAGGU G UCCCCGUC	6791	GACGGGGA GGCTAGCTACAACGA ACCTACAC	15540
1487	GUGUCCCC G UCAACGCC	6792	GGCGTTGA GGCTAGCTACAACGA GGGGACAC	15541
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1481	CCGUCAAC G CCGGCAA	6794	TTTGCCGG GGCTAGCTACAACGA GTTGACGG	15543
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1442	UUAGCCCA G UCCCCAC	6804	GTGGGGAA GGCTAGCTACAACGA TGGGCTAA	15553
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1432	UCCCCACC A UGGAUUA	6806	TTATTCCA GGCTAGCTACAACGA GGTGGGGA	15555
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1424	AUGGAUA A UAGGCAAG	6808	CTTGCCTA GGCTAGCTACAACGA TATTCCAT	15557
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1387	GGGCCCC G CCACCAUG	6815	CATGGTGG GGCTAGCTACAACGA GGGGGCCC	15564
1384	CCCCCGC A CCAUGUCC	6816	GGACATGG GGCTAGCTACAACGA GGCGGGGG	15565
1381	CCGCCACC A UGUCCACG	6817	CGTGGACA GGCTAGCTACAACGA GGTGGCGG	15566
1379	GCCACCAU G UCCACGAC	6818	GTCGTGGA GGCTAGCTACAACGA ATGGTGGC	15567
1375	CCAUGUCC A CGACGGCU	6819	AGCCGTGG GGCTAGCTACAACGA GGACATGG	15568
1372	UGUCCACG A CGGCUUGU	6820	ACAAGCCG GGCTAGCTACAACGA CGTGGACA	15569
1369	CCACGACG G CUUGUGGG	6821	CCCACAAG GGCTAGCTACAACGA CGTCGTGG	15570
1365	GACGGCUU G UGGGAUCC	6822	GGATCCCA GGCTAGCTACAACGA AAGCCGTC	15571
1360	CUUGUGGG A UCCGGAGC	6823	GCTCCGGA GGCTAGCTACAACGA CCCACAAG	15572
1353	GAUCCGGA G CAACUGCG	6824	CGCAGTTG GGCTAGCTACAACGA TCCGGATC	15573
1350	CCGGAGCA A CUGCGAUA	6825	TATCGCAG GGCTAGCTACAACGA TGCTCCGG	15574

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1344	CAACUGCG A UACCACUA	6827	TAGTGGTA GGCTAGCTACAACGA CGCAGTTG	15576
1342	ACUGCGAU A CCACUAGG	6828	CCTAGTGG GGCTAGCTACAACGA ATCGCAGT	15577
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1333	CCACUAGG G CUGUUGUA	6830	TACAACAG GGCTAGCTACAACGA CCTAGTGG	15579
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1323	UGUUGUAG G UGACCAAU	6833	ATTGGTCA GGCTAGCTACAACGA CTACAACA	15582
1320	UGUAGGUG A CCAAUUCA	6834	TGAATTGG GGCTAGCTACAACGA CACCTACA	15583
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1292	CAAGCCAU G CGAUGGCC	6842	GGCCATCG GGCTAGCTACAACGA ATGGCTTG	15591
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1286	AUGCGAUG G CCUGAUAC	6844	GTATCAGG GGCTAGCTACAACGA CATCGCAT	15593
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1277	CCUGAUAC G UGGCCGGG	6847	CCCGGCCA GGCTAGCTACAACGA GTATCAGG	15596
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1268	UGGCCGGG A UAGAUCGA	6849	TCGATCTA GGCTAGCTACAACGA CCCGGCCA	15598
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1216	GCGAGAAG G UGAACAGC	6862	GCTGTTC A GGCTAGCTACAACGA CTTCTCGC	15611
1212	GAAGGUGA A CAGCUGAG	6863	CTCAGCTG GGCTAGCTACAACGA TCACCTTC	15612
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1184	ACAGAUCG G CAGAGAUC	6868	GATCTCTG GGCTAGCTACAACGA GGATCTGT	15617
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1167	CCCCACGU A CAUAGCAG	6872	CTGCTATG GGCTAGCTACAACGA ACGTGGGG	15621
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1150	AGCAGAAA G CAGCCGCC	6876	GGCGCTG GGCTAGCTACAACGA TTTCTGCT	15625
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1138	CCGCCCCA A CGAGCAAA	6879	TTTGCTCG GGCTAGCTACAACGA TGGGGCGG	15628
1134	CCCAACGA G CAAAUCCA	6880	TCGATTTG GGCTAGCTACAACGA TCGTTGGG	15629
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1121	UCGACGUG A CGCCGUAU	6884	ATACGCGG GGCTAGCTACAACGA CACGTCGA	15633
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1116	GUGACGCC G UAUCGUCG	6886	CGACGATA GGCTAGCTACAACGA GGCGTCAC	15635
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1097	GUGGGGAU G CUGGCAUU	6892	AATGCCAG GGCTAGCTACAACGA ATCCCCAC	15641
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1040	GAGGAGUU G UUCUCCCG	6906	CGGGAGAA GGCTAGCTACAACGA AACTCCTC	15655
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1019	CAGGGCAC G CACCCCGG	6911	CCGGGGTG GGCTAGCTACAACGA GTGCCCTG	15660
1017	GGGCACGC A CCCCAGGG	6912	CCCCGGGG GGCTAGCTACAACGA GCGTGCCC	15661
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1007	CCCGGGGU G UGCAUGAU	6914	ATCATGCA GGCTAGCTACAACGA ACCCGGGG	15663
1005	CGGGGUGU G CAUGAUCA	6915	TGATCATG GGCTAGCTACAACGA ACACCCCG	15664
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995	AUGAUCAU G UCCUCUGC	6919	GCAGAGGA GGCTAGCTACAACGA ATGATCAT	15668
988	UGUCCUCU G CCUCAUAC	6920	GTATGAGG GGCTAGCTACAACGA AGAGGACA	15669
983	UCUGCCUC A UACACAAU	6921	ATTGTGTA GGCTAGCTACAACGA GAGGCAGA	15670
981	UGCCUCAU A CACAAUGC	6922	GCATTGTG GGCTAGCTACAACGA ATGAGGCA	15671
979	CCUCAUAC A CAAUGCUU	6923	AAGCATTG GGCTAGCTACAACGA GTATGAGG	15672
976	CAUACACA A UGUUGAG	6924	CTCAAGCA GGCTAGCTACAACGA TGTGTATG	15673
974	UACACAAU G CUUGAGUU	6925	AACTCAAG GGCTAGCTACAACGA ATTGTGTA	15674
968	AUGCUUGA G UUGGAGCA	6926	TGCTCCAA GGCTAGCTACAACGA TCAAGCAT	15675
962	GAGUUGGA G CAAUCGUU	6927	AACGATTG GGCTAGCTACAACGA TCCAATC	15676
959	UUGGAGCA A UCGUUCGU	6928	ACGAACGA GGCTAGCTACAACGA TGCTCCAA	15677
956	GAGCAAUC G UUCGUGAC	6929	GTCACGAA GGCTAGCTACAACGA GATTGCTC	15678
952	AAUCGUUC G UGACAUUG	6930	CCATGTCA GGCTAGCTACAACGA GAACGATT	15679
949	CGUUCGUG A CAUGGUAC	6931	GTACCATG GGCTAGCTACAACGA CACGAACG	15680
947	UUCGUGAC A UGGUACAG	6932	CTGTACCA GGCTAGCTACAACGA GTCACGAA	15681
944	GUGACAUG G UACAGCCC	6933	GGGCTGTA GGCTAGCTACAACGA CATGTCAC	15682
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939	AUGGUACA G CCCGGACG	6935	CGTCCGGG GGCTAGCTACAACGA TGTACCAT	15684
933	CAGCCCGG A CGCGUUGC	6936	GCAACGCG GGCTAGCTACAACGA CCGGGCTG	15685
931	GCCCCGAC G CGUUGCAC	6937	GTGCAACG GGCTAGCTACAACGA GTCCGGGC	15686

929	CCGGACGC G UUGCACAC	6938	GTGTGCAA GGCTAGCTACAACGA GCGTCCGG	15687
926	GACGCGUU G CACACCUC	6939	GAGGTGTG GGCTAGCTACAACGA AACGCGTC	15688
924	CGCGUUGC A CACCUCAU	6940	ATGAGGTG GGCTAGCTACAACGA GCAACGCG	15689
922	CGUUGCAC A CCUCAUAA	6941	TTATGAGG GGCTAGCTACAACGA GTGCAACG	15690
917	CACACCUC A UAAGCGGA	6942	TCCGCTTA GGCTAGCTACAACGA GAGGTGTG	15691
913	CCUCAUAA G CGGAGGCU	6943	AGCCTCCG GGCTAGCTACAACGA TTATGAGG	15692
907	AAGCGGAG G CUGGGAUG	6944	CATCCCAG GGCTAGCTACAACGA CTCGCTT	15693
901	AGGCGGG A UGGUCAGA	6945	TCTGACCA GGCTAGCTACAACGA CCCAGCCT	15694
898	CUGGGAUG G UCAGACAG	6946	CTGTCTGA GGCTAGCTACAACGA CATCCCAG	15695
893	AUGGUCAG A CAGGGCAG	6947	CTGCCCTG GGCTAGCTACAACGA CTGACCAT	15696
888	CAGACAGG G CAGCAGAG	6948	CTCTGCTG GGCTAGCTACAACGA CCTGTCTG	15697
885	ACAGGGCA G CAGAGCCA	6949	TGGCTCTG GGCTAGCTACAACGA TGCCCTGT	15698
880	GCAGCAGA G CCAAGAGG	6950	CCTCTTGG GGCTAGCTACAACGA TCTCTGTC	15699
868	AGAGGAAG A UAGAGAAA	6951	TTTCTCTA GGCTAGCTACAACGA CTTCTCT	15700
857	GAGAAAGA G CAACCGGG	6952	CCCGGTTG GGCTAGCTACAACGA TCTTCTC	15701
854	AAAGAGCA A CCGGGCAG	6953	CTGCCCGG GGCTAGCTACAACGA TGCTCTT	15702
849	GCAACCGG G CAGAUUCC	6954	GGAATCTG GGCTAGCTACAACGA CCGGTTGC	15703
845	CCGGGCAG A UGCCUGU	6955	ACAGGGAA GGCTAGCTACAACGA CTGCCCGG	15704
838	GAUUCCCU G UUGCAUAG	6956	CTATGCAA GGCTAGCTACAACGA AGGGAATC	15705
835	UCCUGUU G CAUAGUUC	6957	GAACTATG GGCTAGCTACAACGA AACAGGGA	15706
833	CCUGUUGC A UAGUUCAC	6958	GTGAACTA GGCTAGCTACAACGA GCAACAGG	15707
830	GUUGCAUA G UUCACGCC	6959	GGCGTGAA GGCTAGCTACAACGA TATGCAAC	15708
826	CAUAGUUC A CGCCGUCU	6960	AGACGGCG GGCTAGCTACAACGA GAACTATG	15709
824	UAGUUCAC G CCGUCUUC	6961	GAAGACGG GGCTAGCTACAACGA GTGAACTA	15710
821	UUCACGCC G UCUUCCAG	6962	CTGGAAGA GGCTAGCTACAACGA GCGGTGAA	15711
811	CUUCCAGA A CCCGACG	6963	CGTCCGGG GGCTAGCTACAACGA TCTGGAAG	15712
805	GAACCCCG A CGCAUGC	6964	GCATGGCG GGCTAGCTACAACGA CCGGGTTC	15713
803	ACCCGGAC G CCAUGC GC	6965	GCGCATGG GGCTAGCTACAACGA GTCCGGGT	15714
800	CGGACGCC A UGCGCCAG	6966	CTGGCGCA GGCTAGCTACAACGA GCGTCCG	15715
798	GACGCCAU G CGCCAGGG	6967	CCCTGGCG GGCTAGCTACAACGA ATGGCGTC	15716
796	CGCCAUGC G CCAGGGCC	6968	GGCCCTGG GGCTAGCTACAACGA GCATGGCG	15717
790	GCGCCAGG G CCCUGGCA	6969	TGCCAGGG GGCTAGCTACAACGA CCTGGCGC	15718
784	GGGCCUG G CAGUGCCU	6970	AGGCACTG GGCTAGCTACAACGA CAGGGCCC	15719
781	CCCUGCCA G UGCCUCCC	6971	GGGAGGCA GGCTAGCTACAACGA TGCCAGGG	15720
779	CUGGCAGU G CCUCCCAA	6972	TTGGGAGG GGCTAGCTACAACGA ACTGCCAG	15721
766	CCAAGGGG G CGCCGACG	6973	CGTCGGCG GGCTAGCTACAACGA CCCCTTGG	15722
764	AAGGGGGC G CCGACGAG	6974	CTCGTCGG GGCTAGCTACAACGA GCCCCTT	15723
760	GGGCGCCG A CGAGCGGA	6975	TCCGCTCG GGCTAGCTACAACGA CGGCGCCC	15724
756	GCCGACGA G CGGAAUGU	6976	ACATTCCG GGCTAGCTACAACGA TCGTCGGC	15725
751	CGAGCGGA A UGUACCCC	6977	GGGGTACA GGCTAGCTACAACGA TCCGCTCG	15726
749	AGCGGAU G UACCCAU	6978	ATGGGGTA GGCTAGCTACAACGA ATTCCGCT	15727
747	CGGAUUGU A CCCCAUGA	6979	TCATGGGG GGCTAGCTACAACGA ACATTCCG	15728
742	UGUACCCC A UGAGGUCG	6980	CGACCTCA GGCTAGCTACAACGA GGGGTACA	15729
737	CCCAUGAG G UCGGCGAA	6981	TTCGCCGA GGCTAGCTACAACGA CTCATGGG	15730
733	UGAGGUCG G CGAAGCCG	6982	CGGCTTCG GGCTAGCTACAACGA CGACCTCA	15731
728	UCGGCGAA G CCGCAUGU	6983	ACATGCGG GGCTAGCTACAACGA TCGCCGA	15732
725	GCGAAGCC G CAUGUGAG	6984	CTCACATG GGCTAGCTACAACGA GGCTTCGC	15733
723	GAAGCCGC A UGUGAGGG	6985	CCCTCACA GGCTAGCTACAACGA GCGGCTTC	15734
721	AGCCGCAU G UGAGGGUA	6986	TACCTCA GGCTAGCTACAACGA ATGCGGCT	15735
715	AUGUGAGG G UAUUGAUG	6987	CATCGATA GGCTAGCTACAACGA CCTCACAT	15736
713	GUGAGGGU A UCGAUGAC	6988	GTCATCGA GGCTAGCTACAACGA ACCCTCAC	15737
709	GGGUAUCG A UGACCUUA	6989	TAAGGTCA GGCTAGCTACAACGA CGATACCC	15738
706	UAUCGAUG A CCUUAACC	6990	GGGTAAGG GGCTAGCTACAACGA CATCGATA	15739
701	AUGACCUU A CCCAAGUU	6991	AACTTGGG GGCTAGCTACAACGA AAGGTCAT	15740
695	UUACCCAA G UUACGCGA	6992	TCGCGTAA GGCTAGCTACAACGA TTGGGTAA	15741
692	CCCAAGUU A CGCGACCU	6993	AGGTCGCG GGCTAGCTACAACGA AACTTGGG	15742

690	CAAGUAC G CGACCUAC	6994	GTAGGTCG GGCTAGCTACAACGA GTAACCTG	15743
687	GUUACGCG A CCUACGCC	6995	GGCGTAGG GGCTAGCTACAACGA CGCGTAAC	15744
683	CGCGACCU A CGCGGGG	6996	CCCCGGCG GGCTAGCTACAACGA AGGTGCGG	15745
681	CGACCUAC G CCGGGGGU	6997	ACCCCGG GGCTAGCTACAACGA GTAGGTCG	15746
674	CGCGGGG G UCCUGGG	6998	CCCACGGA GGCTAGCTACAACGA CCGGGCG	15747
670	GGGGGUCC G UGGGGCCC	6999	GGGCCCCA GGCTAGCTACAACGA GGACCCC	15748
665	UCCUGGG G CCCCAACU	7000	AGTTGGGG GGCTAGCTACAACGA CCCACGGA	15749
659	GGGCCCCA A CUAGGCCG	7001	CGGCCTAG GGCTAGCTACAACGA TGGGGCCC	15750
654	CCAACUAG G CCGGGAGC	7002	GCTCCCGG GGCTAGCTACAACGA CTAGTTGG	15751
647	GGCCGGGA G CCGGGGG	7003	CCCCGGG GGCTAGCTACAACGA TCCGGGCC	15752
644	CGGGAGCC G CGGGGUGA	7004	TCACCCCG GGCTAGCTACAACGA GGCTCCCG	15753
639	GCCGCGGG G UGACAGGA	7005	TCCTGTCA GGCTAGCTACAACGA CCGCGGC	15754
636	GCGGGGUG A CAGGAGCC	7006	GGCTCCTG GGCTAGCTACAACGA CACCCCGC	15755
630	UGACAGGA G CCAUCCUG	7007	CAGGATGG GGCTAGCTACAACGA TCCTGTCA	15756
627	CAGGAGCC A UCCUGCCC	7008	GGGCAGGA GGCTAGCTACAACGA GGCTCCTG	15757
622	GCCAUCCU G CCCACCCU	7009	AGGGTGGG GGCTAGCTACAACGA AGGATGGC	15758
618	UCCUGCCC A CCCUAAGC	7010	GCTTAGGG GGCTAGCTACAACGA GGGCAGGA	15759
611	CACCCUAA G CCCUCAU	7011	AATGAGGG GGCTAGCTACAACGA TTAGGGTG	15760
605	AAGCCUC A UUGCCAUA	7012	TATGGCAA GGCTAGCTACAACGA GAGGGCTT	15761
602	CCCUCAU G CCAUAGAG	7013	CTCTATGG GGCTAGCTACAACGA AATGAGGG	15762
599	UCAUUGCC A UAGAGGGG	7014	CCCTCTA GGCTAGCTACAACGA GGCAATGA	15763
591	AUAGAGGG G CCAAGGGU	7015	ACCTTGG GGCTAGCTACAACGA CCCTCTAT	15764
584	GGCCAAGG G UACCCGGG	7016	CCCGGGTA GGCTAGCTACAACGA CCTTGGCC	15765
582	CCAAGGGU A CCCGGGCU	7017	AGCCCGGG GGCTAGCTACAACGA ACCCTTGG	15766
576	GUACCCGG G CUGAGCCC	7018	GGGCTCAG GGCTAGCTACAACGA CCGGGTAC	15767
571	CGGGCUGA G CCAGGCC	7019	GGCCTGGG GGCTAGCTACAACGA TCAGCCCG	15768
565	GAGCCCAG G CCCUGCCC	7020	GGGCAGGG GGCTAGCTACAACGA CTGGGCTC	15769
560	CAGGCCCU G CCCUGGG	7021	CCCGAGGG GGCTAGCTACAACGA AGGGCCTG	15770
552	GCCCUCGG G CCGGCGAG	7022	CTCGCCGG GGCTAGCTACAACGA CCGAGGGC	15771
548	UCGGGCCG G CGAGCCUU	7023	AAGGCTCG GGCTAGCTACAACGA CGGCCCGA	15772
544	GCCGGCGA G CCUUGGGG	7024	CCCCAAGG GGCTAGCTACAACGA TCGCCGGC	15773
535	CCUUGGGG A UAGGUUGU	7025	ACAACCTA GGCTAGCTACAACGA CCCCAGG	15774
531	GGGGAUAG G UUGCGCC	7026	GGCGACAA GGCTAGCTACAACGA CTATCCCC	15775
528	GAUAGGUU G UGCGCUUC	7027	GAAGCGGA GGCTAGCTACAACGA AACCTATC	15776
525	AGGUUGUC G CCUCCAC	7028	GTGGAAGG GGCTAGCTACAACGA GACAACCT	15777
518	CGCCUUC A CGAGGUUG	7029	CAACCTCG GGCTAGCTACAACGA GGAAGGCG	15778
513	UCCACGAG G UUGCGACC	7030	GGTCGCAA GGCTAGCTACAACGA CTCGTGGA	15779
510	ACGAGGUU G CGACCGCU	7031	AGCGGTCG GGCTAGCTACAACGA AACCTCGT	15780
507	AGGUUGCG A CCGCUCGG	7032	CCGAGCGG GGCTAGCTACAACGA CGCAACCT	15781
504	UUGCGACC G CUCGGAAG	7033	CTTCCGAG GGCTAGCTACAACGA GGTCGCAA	15782
496	GCUCGGAA G UCUUCCUA	7034	TAGGAAGA GGCTAGCTACAACGA TTCCGAGC	15783
487	UCUUCCUA G UCGCGCGC	7035	GCGCGCGA GGCTAGCTACAACGA TAGGAAGA	15784
484	UCCUAGUC G CGCGACA	7036	TGTGCGCG GGCTAGCTACAACGA GACTAGGA	15785
482	CUAGUCGC G CGCACACC	7037	GGTGTGCG GGCTAGCTACAACGA GCGACTAG	15786
480	AGUCGCGC G CACACCCA	7038	TGGGTGTG GGCTAGCTACAACGA GCGCGACT	15787
478	UCGCGCGC A CACCCAAC	7039	GTTGGGTG GGCTAGCTACAACGA GCGCGCGA	15788
476	GCGCGCAC A CCCAACCU	7040	AGGTTGGG GGCTAGCTACAACGA GTGCGCGC	15789
471	CACACCCA A CCUGGGGC	7041	GCCCCAGG GGCTAGCTACAACGA TGGGTGTG	15790
464	AACCUGGG G CCCCUGCG	7042	CGCAGGGG GGCTAGCTACAACGA CCCAGGTT	15791
458	GGGCCCCU G CGCGCAA	7043	TGCGCGCG GGCTAGCTACAACGA AGGGGCC	15792
456	GCCCCUGC G CGGCAACA	7044	TGTTGCCG GGCTAGCTACAACGA GCAGGGGC	15793
453	CCUGCGCG G CAACAGGU	7045	ACCTGTTG GGCTAGCTACAACGA CGCGCAGG	15794
450	GCGCGGCA A CAGGUAAA	7046	TTTACCTG GGCTAGCTACAACGA TGCCGCGC	15795
446	GGCAACAG G UAAACUCC	7047	GGAGTTTA GGCTAGCTACAACGA CTGTTGCC	15796
442	ACAGGUAA A CUCCACCA	7048	TGGTGGAG GGCTAGCTACAACGA TTACCTGT	15797
437	UAAACUCC A CCAACGAU	7049	ATCGTTGG GGCTAGCTACAACGA GGAGTTTA	15798

433	CUCCACCA A CGAUCUGA	7050	TCAGATCG GGCTAGCTACAACGA TGGTGGAG	15799
430	CACCAACG A UCUGACCA	7051	TGGTCAGA GGCTAGCTACAACGA CGTTGGTG	15800
425	ACGAUCUG A CCACCGCC	7052	GGCGGTGG GGCTAGCTACAACGA CAGATCGT	15801
422	AUCUGACC A CCGCCCGG	7053	CCGGGCGG GGCTAGCTACAACGA GGTGAGAT	15802
419	UGACCACC G CCCGGGAA	7054	TTCCCGGG GGCTAGCTACAACGA GGTGGTCA	15803
411	GCCCGGGA A CUUGACGU	7055	ACGTCAAG GGCTAGCTACAACGA TCCCGGGC	15804
406	GGAACUUG A CGUCCUGU	7056	ACAGGACG GGCTAGCTACAACGA CAAGTTCC	15805
404	AACUUGAC G UCCUGUGG	7057	CCACAGGA GGCTAGCTACAACGA GTCAAGTT	15806
399	GACGUCCU G UGGGCGGC	7058	GCCGCCCA GGCTAGCTACAACGA AGGACGTC	15807
395	UCCUGUGG G CGGCGGUU	7059	AACCGCCG GGCTAGCTACAACGA CCACAGGA	15808
392	UGUGGGCG G CGGUUGGU	7060	ACCAACCG GGCTAGCTACAACGA CGCCACA	15809
389	GGGCGGCG G UUGGUGUU	7061	AACACCAA GGCTAGCTACAACGA CGCCGCC	15810
385	GGCGGUUG G UGUUACGU	7062	ACGTAACA GGCTAGCTACAACGA CAACCGCC	15811
383	CGGUUGGU G UUACGUUU	7063	AAACGTAA GGCTAGCTACAACGA ACCAACCG	15812
380	UUGGUGUU A CGUUGGUU	7064	ACCAAACG GGCTAGCTACAACGA AACACCAA	15813
378	GGUGUUAC G UUUGGUUU	7065	AAACCAAA GGCTAGCTACAACGA GTAACACC	15814
373	UACGUUUG G UUUUUCUU	7066	AAGAAAAA GGCTAGCTACAACGA CAAACGTA	15815
360	UCUUUGAG G UUUAGGAU	7067	ATCCTAAA GGCTAGCTACAACGA CTCAAAGA	15816
353	GGUUUAGG A UUCGUGCU	7068	AGCACGAA GGCTAGCTACAACGA CCTAAACC	15817
349	UAGGAUUC G UGCUCAUG	7069	CATGAGCA GGCTAGCTACAACGA GAATCCTA	15818
347	GGAUUCGU G CUCAUGGU	7070	ACCATGAG GGCTAGCTACAACGA ACGAATCC	15819
343	UCGUGCUC A UGGUGCAC	7071	GTGCACCA GGCTAGCTACAACGA GAGCACGA	15820
340	UGCUCAUG G UGCACGGU	7072	ACCGTGCA GGCTAGCTACAACGA CATGAGCA	15821
338	CUCAUGGU G CACGGUCU	7073	AGACCGTG GGCTAGCTACAACGA ACCATGAG	15822
336	CAUGGUGC A CGGUCUAC	7074	GTAGACCG GGCTAGCTACAACGA GCACCATG	15823
333	GGUGCACG G UCUACGAG	7075	CTCGTAGA GGCTAGCTACAACGA CGTGCACC	15824
329	CACGGUCU A CGAGACCU	7076	AGGTCTCG GGCTAGCTACAACGA AGACCGTG	15825
324	UCUACGAG A CCUCCCGG	7077	CCGGGAGG GGCTAGCTACAACGA CTCGTAGA	15826
314	CUCCCGGG G CACUCGCA	7078	TGCGAGTG GGCTAGCTACAACGA CCCGGGAG	15827
312	CCCGGGGC A CUCGCAAG	7079	CTTGCGAG GGCTAGCTACAACGA GCCCGGG	15828
308	GGGCACUC G CAAGCACC	7080	GGTGCTTG GGCTAGCTACAACGA GAGTGCCC	15829
304	ACUCGCAA G CACCCUAU	7081	ATAGGGTG GGCTAGCTACAACGA TTGCGAGT	15830
302	UCGCAAGC A CCCUAUCA	7082	TGATAGGG GGCTAGCTACAACGA GCTTGCGA	15831
297	AGCACCCU A UCAGGCAG	7083	CTGCCTGA GGCTAGCTACAACGA AGGGTGCT	15832
292	CCUAUCAG G CAGUACCA	7084	TGGTACTG GGCTAGCTACAACGA CTGATAGG	15833
289	AUCAGGCA G UACCACAA	7085	TTGTGGTA GGCTAGCTACAACGA TGCCTGAT	15834
287	CAGGCAGU A CCACAAGG	7086	CCTTGTGG GGCTAGCTACAACGA ACTGCCTG	15835
284	GCAGUACC A CAAGGCCU	7087	AGGCCTTG GGCTAGCTACAACGA GGTACTGC	15836
279	ACCACAAG G CCUUUCGC	7088	GCGAAAGG GGCTAGCTACAACGA CTGTGGT	15837
272	GGCCUUUC G CGACCCAA	7089	TTGGGTGCG GGCTAGCTACAACGA GAAAGGCC	15838
269	CUUUCGCG A CCCAACAC	7090	GTGTTGGG GGCTAGCTACAACGA CGCGAAAG	15839
264	GCGACCCA A CACUACUC	7091	GAGTAGTG GGCTAGCTACAACGA TGGGTCGC	15840
262	GACCCAAC A CUACUCGG	7092	CCGAGTAG GGCTAGCTACAACGA GTGGGTC	15841
259	CCAACACU A CUCGGCUA	7093	TAGCCGAG GGCTAGCTACAACGA AGTGTGG	15842
254	ACUACUCG G CUAGCAGU	7094	ACTGCTAG GGCTAGCTACAACGA CGAGTAGT	15843
250	CUCGGCUA G CAGUCUCG	7095	CGAGACTG GGCTAGCTACAACGA TAGCCGAG	15844
247	GGCUAGCA G UCUCGCGG	7096	CCGCGAGA GGCTAGCTACAACGA TGCTAGCC	15845
242	GCAGUCUC G CGGGGGCA	7097	TGCCCCCG GGCTAGCTACAACGA GAGACTGC	15846
236	UCGCGGGG G CACGCCCA	7098	TGGGCGTG GGCTAGCTACAACGA CCCC CGA	15847
234	GCGGGGGC A CGCCCAA	7099	TTTGGCGG GGCTAGCTACAACGA GCCCCCGC	15848
232	GGGGGGAC G CCCC AAUC	7100	GATTGGGG GGCTAGCTACAACGA GTGCCCCC	15849
226	ACGCCCAA A UCUC CAGG	7101	CCTGGAGA GGCTAGCTACAACGA TTGGCGGT	15850
218	AUCUCCAG G CAUUGAGC	7102	GCTCAATG GGCTAGCTACAACGA CTGGAGAT	15851
216	CUCCAGGC A UUGAGCGG	7103	CCGCTCAA GGCTAGCTACAACGA GCCTGGAG	15852
211	GGCAUUGA G CGGGUUGA	7104	TCAACCCG GGCTAGCTACAACGA TCAATGCC	15853
207	UUGAGCGG G UUGAUCCA	7105	TGGATCAA GGCTAGCTACAACGA CCGCTCAA	15854

203	GCGGGUUG A UCCAAGAA	7106	TTCTTGGA GGCTAGCTACAACGA CAACCCGC	15855
191	AAGAAAGG A CCGGUCG	7107	CGACCGGG GGCTAGCTACAACGA CCTTTCTT	15856
186	AGGACCGG G UCGUCCUG	7108	CAGGACGA GGCTAGCTACAACGA CGGGTCCT	15857
183	ACCCGGUC G UCCUGGCA	7109	TGCCAGGA GGCTAGCTACAACGA GACCGGGT	15858
177	UCGUCCUG G CAAUCCG	7110	CGGAATTG GGCTAGCTACAACGA CAGGACGA	15859
174	UCCUGGCA A UCCGGUG	7111	CACCGGAA GGCTAGCTACAACGA TGCCAGGA	15860
168	CAAUCCG G UGUACUCA	7112	TGAGTACA GGCTAGCTACAACGA CGGAATTG	15861
166	AUCCGGU G UACUACC	7113	GGTGAGTA GGCTAGCTACAACGA ACCGGAAT	15862
164	UCCGGUGU A CUCACCG	7114	CCGGTGAG GGCTAGCTACAACGA ACACCGGA	15863
160	GUGUACUC A CCGUUCC	7115	GGAACCGG GGCTAGCTACAACGA GAGTACAC	15864
156	ACUCACCG G UUCGCGAG	7116	CTGCGGAA GGCTAGCTACAACGA CGGTGAGT	15865
151	CCGGUUC G CAGACCAC	7117	GTGGTCTG GGCTAGCTACAACGA GGAACCGG	15866
147	UCCGCGAG A CCACUAG	7118	CATAGTGG GGCTAGCTACAACGA CTGCGGAA	15867
144	CGCAGACC A CUAUGGCU	7119	AGCCATAG GGCTAGCTACAACGA GGTCTGCG	15868
141	AGACCACU A UGGCUCUC	7120	GAGAGCCA GGCTAGCTACAACGA AGTGGTCT	15869
138	CCACUAG G CUCUCCG	7121	CGGGAGAG GGCTAGCTACAACGA CATAGTGG	15870
120	GAGGGGGG G UCCUGGAG	7122	CTCCAGGA GGCTAGCTACAACGA CCCCCCTC	15871
111	UCCUGGAG G CUGCACGA	7123	TCGTGCAG GGCTAGCTACAACGA CTCCAGGA	15872
108	UGGAGGCU G CACGACAC	7124	GTGTCTGT GGCTAGCTACAACGA AGCCTCCA	15873
106	GAGGCUGC A CGACACUC	7125	GAGTGTCT GGCTAGCTACAACGA GCAGCCTC	15874
103	GCUGCACG A CACUCAUA	7126	TATGAGTG GGCTAGCTACAACGA CGTGCAGC	15875
101	UGCACGAC A CUCAUACU	7127	AGTATGAG GGCTAGCTACAACGA GTCGTGCA	15876
97	CGACACUC A UACUACG	7128	CGTTAGTA GGCTAGCTACAACGA GAGTGTCT	15877
95	ACACUCAU A CUAACGCC	7129	GGCGTTAG GGCTAGCTACAACGA ATGAGTGT	15878
91	UCAUACUA A CGCAUGG	7130	CCATGGCG GGCTAGCTACAACGA TAGTATGA	15879
89	AUACUAC G CCAUGGCU	7131	AGCCATGG GGCTAGCTACAACGA GTAGTAT	15880
86	CUAACGCC A UGGCUAGA	7132	TCTAGCCA GGCTAGCTACAACGA GGCCTTAG	15881
83	ACGCCAUG G CUAGACGC	7133	GCGTCTAG GGCTAGCTACAACGA CATGGCGT	15882
78	AUGGCUAG A CGCUUUCU	7134	AGAAAGCG GGCTAGCTACAACGA CTAGCCAT	15883
76	GGCUAGAC G CUUUCUGC	7135	GCAGAAAG GGCTAGCTACAACGA GTCTAGCC	15884
69	CGCUUUCU G CGUGAAGA	7136	TCTTCACG GGCTAGCTACAACGA AGAAAGCG	15885
67	CUUUCUGC G UGAAGACA	7137	TGTCTTCA GGCTAGCTACAACGA GCAGAAAG	15886
61	GCGUGAAG A CAGUAGUU	7138	AACTACTG GGCTAGCTACAACGA CTTCACGC	15887
58	UGAAGACA G UAGUCCU	7139	AGGAACCTA GGCTAGCTACAACGA TGTCTTCA	15888
55	AGACAGUA G UUCUCAC	7140	GTGAGGAA GGCTAGCTACAACGA TACTGTCT	15889
48	AGUUCUC A CAGGGGAG	7141	CTCCCTTG GGCTAGCTACAACGA GAGGAACT	15890
40	ACAGGGGA G UGAUCUAA	7142	ATAGATCA GGCTAGCTACAACGA TCCCCTGT	15891
37	GGGGAGUG A UCUAUGGU	7143	ACCATAGA GGCTAGCTACAACGA CACTCCCC	15892
33	AGUGAUCU A UGGUGGAG	7144	CTCCACCA GGCTAGCTACAACGA AGATCACT	15893
30	GAUCUAUG G UGGAGUGU	7145	ACACTCCA GGCTAGCTACAACGA CATAGATC	15894
25	AUGGUGGA G UGUCGCC	7146	GGGCGACA GGCTAGCTACAACGA TCCACCAT	15895
23	GGUGGAGU G UGCCCCC	7147	GGGGGCGA GGCTAGCTACAACGA ACTCCACC	15896

Input Sequence = HPCK1S1. Cut Site = R/Y

Arm Length = 8. Core Sequence = GGCTAGCTACAACGA

HPCK1S1 Hepatitis C virus (strain HCV-1b, clone HCV-K1-S1), complete genome; acc#
gi|1030702|dbj|D50483.1; 9410 nt

Table XX: Synthetic anti-HCV nucleic acid molecule and Target Sequences

ref pos	Ref Seq	Target	Seq ID	RPI#	NUCLEIC ACID	Seq ID	Nucleic Acid Alias
195	HCV+	GGGUCCU U UCUUGGA	7148	15364	C ₈ C ₈ A ₈ A ₈ G ₈ CUGAUGAGggcgaaagccGaa Aggacc B	15897	Hammerhead
342	HCV+	AGACCGUGCAUGAGCAC	7149	17501	G ₈ T ₈ G ₈ C ₈ T ₈ C ₈ A ₈ T ₈ G ₈ A ₈ T ₈ G ₈ C ₈ A ₈ C ₈ G ₈ T ₈ C ₈ T	15898	Antisense
195	HCV+	GGGUCCU U UCUUGGA	7148	17558	C ₈ C ₈ A ₈ A ₈ G ₈ CUGAUGAGggcguaagccGaz Aggacc B	15899	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	17559	C ₈ C ₈ A ₈ A ₈ G ₈ CUGAUGAGggcguaagccGaa AggaZc B	15900	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	17560	Z ₈ C ₈ A ₈ A ₈ G ₈ CUGAUGAGggcguaagccGaa Aggacc B	15901	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	17561	Z ₈ C ₈ A ₈ A ₈ G ₈ CUGAUGAGggcguaagccGaa Aggacc B	15902	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	18012	ccaaga CUGAUGAGggcguaagccGaa Aggacc B	15903	Hammerhead
82	HCV+	CGGUCUA G CCAUGGC	7150	18744	G ₈ C ₈ A ₈ A ₈ U ₈ G ₈ GccgaaagGCGaGucaaGGuCu uagacgc B	15904	Zinzyme
100	HCV+	AGUAUGA G UGUCGUG	7151	18745	C ₈ S ₈ C ₈ S ₈ aca GccgaaagGCGaGucaaGGuCu ucauacu B	15905	Zinzyme
102	HCV+	UAUGAGU G UCGUGCA	7152	18746	u ₈ S ₈ C ₈ A ₈ C ₈ ga GccgaaagGCGaGucaaGGuCu acucaua B	15906	Zinzyme
105	HCV+	GAGUGUC G UGCAGCC	7153	18747	G ₈ S ₈ C ₈ u ₈ gca GccgaaagGCGaGucaaGGuCu gacacuc B	15907	Zinzyme
107	HCV+	GUGUCGU G CAGCCUC	7154	18748	G ₈ A ₈ G ₈ G ₈ cug GccgaaagGCGaGucaaGGuCu acgacac B	15908	Zinzyme
146	HCV+	CAUAGUG G UCUGGG	7155	18749	C ₈ C ₈ S ₈ C ₈ aga GccgaaagGCGaGucaaGGuCu cacuaug B	15909	Zinzyme
190	HCV+	CGACCGG G UCCUUUC	7156	18750	G ₈ A ₈ A ₈ A ₈ gga GccgaaagGCGaGucaaGGuCu ccggucg B	15910	Zinzyme
217	HCV+	GCUCAU G CCUGGAG	7157	18751	C ₈ u ₈ C ₈ S ₈ ag GccgaaagGCGaGucaaGGuCu auugagc B	15911	Zinzyme
231	HCV+	GAUUUG G CGUGCCC	7158	18752	G ₈ S ₈ G ₈ C ₈ acg GccgaaagGCGaGucaaGGuCu ccaaauc B	15912	Zinzyme
258	HCV+	UAGCCGA G UAGUGUU	7159	18753	A ₈ A ₈ C ₈ A ₈ cua GccgaaagGCGaGucaaGGuCu ucggcua B	15913	Zinzyme
307	HCV+	GGUGCUU G CGAGUGC	7160	18754	G ₈ C ₈ A ₈ C ₈ ucg GccgaaagGCGaGucaaGGuCu aagcacc B	15914	Zinzyme
77	HCV+	GAAGC G UCUAGC	7161	18755	G ₈ C ₈ u ₈ A ₈ ga GccgaaagGCGaGucaaGGuCu gcuuuc B	15915	Zinzyme
77	HCV+	AGAAAGC G UCUAGCC	7162	18756	G ₈ S ₈ C ₈ u ₈ aga GccgaaagGCGaGucaaGGuCu gcuuuc B	15916	Zinzyme
88	HCV+	AGCCAU G CGUAGU	7163	18757	A ₈ C ₈ u ₈ A ₈ agc GccgaaagGCGaGucaaGGuCu cauggcu B	15917	Zinzyme
94	HCV+	GGCGUUA G UAUGAGU	7164	18758	A ₈ C ₈ u ₈ C ₈ aua GccgaaagGCGaGucaaGGuCu uaacgcc B	15918	Zinzyme
102	HCV+	AUGAGU G UCGUGC	7165	18759	G ₈ C ₈ A ₈ C ₈ ga GccgaaagGCGaGucaaGGuCu acucau B	15919	Zinzyme
105	HCV+	AGUGUC G UGCAGC	7166	18760	G ₈ C ₈ u ₈ G ₈ ga GccgaaagGCGaGucaaGGuCu gacacu B	15920	Zinzyme
110	HCV+	UCGUGCA G CCUCCAG	7167	18761	C ₈ u ₈ G ₈ G ₈ ag GccgaaagGCGaGucaaGGuCu ugacaga B	15921	Zinzyme
137	HCV+	GGGAGA G CCAUAG	7168	18762	C ₈ u ₈ A ₈ u ₈ gg GccgaaagGCGaGucaaGGuCu ucuccc B	15922	Zinzyme
137	HCV+	CGGGAGA G CCAUAGU	7169	18763	A ₈ C ₈ u ₈ A ₈ ugg GccgaaagGCGaGucaaGGuCu ucucccg B	15923	Zinzyme
146	HCV+	AUAGUG G UCUGCG	7170	18764	C ₈ S ₈ C ₈ A ₈ ga GccgaaagGCGaGucaaGGuCu cacuaa B	15924	Zinzyme
150	HCV+	GUGGUCU G CGGAACC	7171	18765	G ₈ S ₈ u ₈ u ₈ cgg GccgaaagGCGaGucaaGGuCu agaccac B	15925	Zinzyme
176	HCV+	CGGAUU G CCAGGAC	7172	18766	G ₈ u ₈ C ₈ C ₈ ugg GccgaaagGCGaGucaaGGuCu aaauccg B	15926	Zinzyme

190	HCV+	GACCGG G UCCUUU	7173	18767	a ₅ a ₅ a ₅ g ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu ccggu ₅ B	15927	Zinzyme
253	HCV+	CUGCUA G CCGAGU	7174	18768	a ₅ c ₅ u ₅ c ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu uagcag ₅ B	15928	Zinzyme
253	HCV+	ACUGCUA G CCGAGUA	7175	18769	u ₅ a ₅ c ₅ u ₅ g ₅ c ₅ g ₅ GccgaaaGCGGaGucaaGGuCu uagcagu ₅ B	15929	Zinzyme
258	HCV+	AGCCGA G UAGUGU	7176	18770	a ₅ c ₅ a ₅ c ₅ u ₅ GccgaaaGCGGaGucaaGGuCu ucggcu ₅ B	15930	Zinzyme
263	HCV+	GAGUAGU G UUGGGUC	7177	18771	g ₅ a ₅ c ₅ c ₅ caa GccgaaaGCGGaGucaaGGuCu acuacuc ₅ B	15931	Zinzyme
268	HCV+	UGUUGG G UCGCGA	7178	18772	u ₅ c ₅ g ₅ c ₅ g ₅ GccgaaaGCGGaGucaaGGuCu ccaaca ₅ B	15932	Zinzyme
268	HCV+	GUGUUGG G UCGCGAA	7179	18773	u ₅ u ₅ c ₅ g ₅ c ₅ g ₅ GccgaaaGCGGaGucaaGGuCu ccaacac ₅ B	15933	Zinzyme
271	HCV+	UUGGGUC G CGAAAGG	7180	18774	c ₅ c ₅ u ₅ g ₅ u ₅ ucg GccgaaaGCGGaGucaaGGuCu gacccaa ₅ B	15934	Zinzyme
283	HCV+	AGGCCUU G UGGUACU	7181	18775	a ₅ g ₅ a ₅ u ₅ ascca GccgaaaGCGGaGucaaGGuCu aaggccu ₅ B	15935	Zinzyme
286	HCV+	CCUUGUG G UACUGCC	7182	18776	g ₅ g ₅ c ₅ a ₅ gua GccgaaaGCGGaGucaaGGuCu cacaagg ₅ B	15936	Zinzyme
291	HCV+	UGGUACU G CCUGAUA	7183	18777	u ₅ a ₅ u ₅ c ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu aguacca ₅ B	15937	Zinzyme
301	HCV+	UGAUAGG G UGCUUGC	7184	18778	g ₅ c ₅ a ₅ a ₅ gca GccgaaaGCGGaGucaaGGuCu ccuauc ₅ B	15938	Zinzyme
303	HCV+	AUAGGEU G CUUGCGA	7185	18779	u ₅ c ₅ g ₅ c ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu acccuau ₅ B	15939	Zinzyme
60	HCV+	ACUACU G UCUUCA	7186	18780	u ₅ g ₅ a ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu aguagu ₅ B	15940	Zinzyme
60	HCV+	AACUACU G UCUUCAC	7187	18781	g ₅ u ₅ g ₅ g ₅ a ₅ g ₅ GccgaaaGCGGaGucaaGGuCu aguagu ₅ B	15941	Zinzyme
68	HCV+	UCUUCAC G CAGAAAG	7188	18782	c ₅ u ₅ u ₅ u ₅ cug GccgaaaGCGGaGucaaGGuCu gugaaga ₅ B	15942	Zinzyme
75	HCV+	CAGAAA G CGUCUA	7189	18783	u ₅ a ₅ g ₅ a ₅ c ₅ g ₅ GccgaaaGCGGaGucaaGGuCu uuucug ₅ B	15943	Zinzyme
82	HCV+	CGUCUA G CCAUGG	7190	18784	c ₅ c ₅ a ₅ u ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu uagacg ₅ B	15944	Zinzyme
88	HCV+	GCCAU G CGUUG	7191	18785	c ₅ u ₅ a ₅ a ₅ c ₅ g ₅ GccgaaaGCGGaGucaaGGuCu cauggc ₅ B	15945	Zinzyme
90	HCV+	CAUGGC G UUAGUA	7192	18786	u ₅ a ₅ c ₅ u ₅ g ₅ aa GccgaaaGCGGaGucaaGGuCu gccaug ₅ B	15946	Zinzyme
90	HCV+	CCAUGGC G UUAGUAU	7193	18787	a ₅ u ₅ a ₅ c ₅ u ₅ aa GccgaaaGCGGaGucaaGGuCu gccaug ₅ B	15947	Zinzyme
100	HCV+	GUAUGA G UGUCGU	7194	18788	a ₅ c ₅ g ₅ g ₅ a ₅ ca GccgaaaGCGGaGucaaGGuCu ucauac ₅ B	15948	Zinzyme
107	HCV+	UGUCGU G CAGCCU	7195	18789	a ₅ g ₅ g ₅ c ₅ g ₅ ug GccgaaaGCGGaGucaaGGuCu acgaca ₅ B	15949	Zinzyme
110	HCV+	CGUGCA G CCUCCA	7196	18790	u ₅ g ₅ g ₅ a ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu ugcacg ₅ B	15950	Zinzyme
150	HCV+	UGGUCU G CGGAAC	7197	18791	g ₅ u ₅ u ₅ c ₅ g ₅ cg GccgaaaGCGGaGucaaGGuCu agacca ₅ B	15951	Zinzyme
159	HCV+	GGAACCG G UGAGUAC	7198	18792	g ₅ u ₅ a ₅ c ₅ u ₅ ca GccgaaaGCGGaGucaaGGuCu cgguucc ₅ B	15952	Zinzyme
176	HCV+	GGAUUU G CCAGGA	7199	18793	u ₅ c ₅ c ₅ u ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu aaaucc ₅ B	15953	Zinzyme
217	HCV+	CUCAAU G CCUGGA	7200	18794	u ₅ c ₅ c ₅ a ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu auugag ₅ B	15954	Zinzyme
231	HCV+	AUUUGG G CGUGCC	7201	18795	g ₅ g ₅ c ₅ a ₅ g ₅ cg GccgaaaGCGGaGucaaGGuCu ccaauu ₅ B	15955	Zinzyme
261	HCV+	CGAGUA G UGUUGG	7202	18796	c ₅ c ₅ a ₅ g ₅ a ₅ ca GccgaaaGCGGaGucaaGGuCu uacucg ₅ B	15956	Zinzyme
261	HCV+	CCGAGUA G UGUUGGG	7203	18797	c ₅ c ₅ c ₅ a ₅ g ₅ aca GccgaaaGCGGaGucaaGGuCu uacucgg ₅ B	15957	Zinzyme
263	HCV+	AGUAGU G UUGGGU	7204	18798	a ₅ c ₅ c ₅ c ₅ aa GccgaaaGCGGaGucaaGGuCu acuacu ₅ B	15958	Zinzyme
271	HCV+	UGGGUC G CGAAAG	7205	18799	c ₅ u ₅ u ₅ u ₅ g ₅ cg GccgaaaGCGGaGucaaGGuCu gaccca ₅ B	15959	Zinzyme
283	HCV+	GGCCUU G UGGUAC	7206	18800	g ₅ u ₅ a ₅ g ₅ c ₅ g ₅ ca GccgaaaGCGGaGucaaGGuCu aaggcc ₅ B	15960	Zinzyme
291	HCV+	GGUACU G CCUGAU	7207	18801	a ₅ u ₅ g ₅ c ₅ a ₅ g ₅ g ₅ GccgaaaGCGGaGucaaGGuCu aguacc ₅ B	15961	Zinzyme

303	HCV+	UAGGGU G CUUGCG	7208	18802	C ₅ S ₅ C ₅ A ₅ g	GccgaaagCGGaGuaaaGGuGū	acccua B	15962	Zinzyne
307	HCV+	GUGCUU G CGAGUG	7209	18803	C ₅ A ₅ C ₅ u ₅ cg	GccgaaagCGGaGuaaaGGuGū	aagcac B	15963	Zinzyne
323	HCV+	CGGGAG G UCUCGU	7210	18804	a ₅ C ₅ S ₅ A ₅ gA	GccgaaagCGGaGuaaaGGuGū	cucccg B	15964	Zinzyne
323	HCV+	CCGGAG G UCUCGUA	7211	18805	u ₅ A ₅ C ₅ g ₅ aga	GccgaaagCGGaGuaaaGGuGū	cucccgg B	15965	Zinzyne
75	HCV+	GCAGAAA G CGUCUAG	7212	18806	C ₅ u ₅ A ₅ g ₅ acg	GccgaaagCGGaGuaaaGGuGū	uuucugc B	15966	Zinzyne
143	HCV+	GCCAUA G UGGUCU	7213	18807	a ₅ S ₅ A ₅ C ₅ ga	GccgaaagCGGaGuaaaGGuGū	uauggc B	15967	Zinzyne
278	HCV+	GCGAAAG G CCUUGUG	7214	18808	C ₅ A ₅ C ₅ A ₅ agg	GccgaaagCGGaGuaaaGGuGū	uuuucgc B	15968	Zinzyne
163	HCV+	CGGUGA G UACACC	7215	18809	g ₅ g ₅ u ₅ g ₅ ua	GccgaaagCGGaGuaaaGGuGū	ucaccg B	15969	Zinzyne
68	HCV+	CUUCAC G CAGAAA	7216	18810	u ₅ u ₅ u ₅ C ₅ ug	GccgaaagCGGaGuaaaGGuGū	gugaag B	15970	Zinzyne
94	HCV+	GGUUA G UAUGAG	7217	18811	C ₅ u ₅ C ₅ A ₅ ua	GccgaaagCGGaGuaaaGGuGū	uaacgc B	15971	Zinzyne
143	HCV+	AGCCAUA G UGGUCUG	7218	18812	C ₅ A ₅ g ₅ A ₅ cca	GccgaaagCGGaGuaaaGGuGū	uauggcu B	15972	Zinzyne
159	HCV+	GAACCG G UGAGUA	7219	18813	u ₅ A ₅ C ₅ u ₅ ga	GccgaaagCGGaGuaaaGGuGū	cggnuu B	15973	Zinzyne
163	HCV+	CCGGUGA G UACACCG	7220	18814	C ₅ S ₅ g ₅ u ₅ gua	GccgaaagCGGaGuaaaGGuGū	ucaccgg B	15974	Zinzyne
249	HCV+	GAGACU G CUAGCC	7221	18815	g ₅ g ₅ C ₅ u ₅ ag	GccgaaagCGGaGuaaaGGuGū	agucuc B	15975	Zinzyne
249	HCV+	CGAGACU G CUAGCCG	7222	18816	C ₅ S ₅ g ₅ C ₅ uag	GccgaaagCGGaGuaaaGGuGū	agucucg B	15976	Zinzyne
278	HCV+	CGAAAG G CCUUGU	7223	18817	a ₅ C ₅ A ₅ A ₅ agg	GccgaaagCGGaGuaaaGGuGū	uuuucg B	15977	Zinzyne
286	HCV+	CUUGUG G UACUGC	7224	18818	g ₅ C ₅ A ₅ g ₅ ua	GccgaaagCGGaGuaaaGGuGū	cacaag B	15978	Zinzyne
301	HCV+	GAUAGG G UGCUUG	7225	18819	C ₅ A ₅ A ₅ g ₅ ga	GccgaaagCGGaGuaaaGGuGū	ccuauu B	15979	Zinzyne
328	HCV+	GGUCUC G UAGACC	7226	18820	g ₅ g ₅ u ₅ C ₅ ua	GccgaaagCGGaGuaaaGGuGū	gagacc B	15980	Zinzyne
328	HCV+	AGGUCUC G UAGACCG	7227	18821	C ₅ g ₅ g ₅ u ₅ cua	GccgaaagCGGaGuaaaGGuGū	gagaccu B	15981	Zinzyne
335	HCV+	UAGACC G UGCACC	7228	18822	g ₅ g ₅ u ₅ g ₅ ga	GccgaaagCGGaGuaaaGGuGū	ggucua B	15982	Zinzyne
30	C	UAAACCU C AAAGAAA	7229	19108	u ₅ u ₅ u ₅ C ₅ uuu	cUGAuGaggcccguaaggccGaa	Agguuuu B	15983	Hammerhead
48	C	CAAAAGU A ACACCAA	7230	19109	u ₅ u ₅ g ₅ g ₅ ugu	cUGAuGaggcccguaaggccGaa	Acguuug B	15984	Hammerhead
60	C	CAACCGU C GCCCACA	7231	19110	u ₅ g ₅ u ₅ g ₅ ggc	cUGAuGaggcccguaaggccGaa	Acgguug B	15985	Hammerhead
175	C	GAGCGGU C ACAACCU	7232	19111	a ₅ g ₅ g ₅ u ₅ ugu	cUGAuGaggcccguaaggccGaa	Accgcuc B	15986	Hammerhead
374	C	GUAAAGU C AUCGAUA	7233	19112	u ₅ a ₅ u ₅ C ₅ gau	cUGAuGaggcccguaaggccGaa	Accuuac B	15987	Hammerhead
258	S27	UGGUGGUCCAUUAGCCCUAG	7234	22022	u ₅ g ₅ g ₅ u ₅ g ₅ g ₅ c ₅ u ₅ c ₅ A ₅ u ₅ c ₅ A ₅ u ₅ C ₅ u ₅ g ₅ u ₅ A ₅ g ₅ c ₅ A ₅ g ₅ c ₅ u ₅ A ₅ g ₅			15988	Antisense
259	S27	GGUGGUCCAUUAGCCCUAGU	7235	22023	g ₅ g ₅ u ₅ g ₅ g ₅ c ₅ u ₅ c ₅ A ₅ u ₅ c ₅ A ₅ u ₅ C ₅ u ₅ g ₅ u ₅ A ₅ g ₅ c ₅ A ₅ g ₅ c ₅ u ₅ A ₅ g ₅			15989	Antisense
260	S27	GUGGUCCAUUAGCCCUAGUC	7236	22024	g ₅ u ₅ g ₅ g ₅ c ₅ u ₅ c ₅ A ₅ u ₅ c ₅ A ₅ u ₅ C ₅ u ₅ g ₅ u ₅ A ₅ g ₅ c ₅ A ₅ g ₅ c ₅ u ₅ A ₅ g ₅			15990	Antisense
261	S27	UGGUCCAUUAGCCCUAGUCA	7237	22025	u ₅ g ₅ g ₅ g ₅ u ₅ c ₅ A ₅ u ₅ c ₅ A ₅ u ₅ C ₅ u ₅ g ₅ u ₅ A ₅ g ₅ c ₅ A ₅ g ₅ c ₅ u ₅ A ₅ g ₅			15991	Antisense
262	S27	GGUCCAUUAGCCCUAGUCAC	7238	22026	g ₅ g ₅ C ₅ u ₅ C ₅ A ₅ u ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅			15992	Antisense
263	S27	GCUCCAUUAGCCCUAGUCACG	7239	22027	g ₅ C ₅ u ₅ C ₅ A ₅ u ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅			15993	Antisense
264	S27	CUCCAUUAGCCCUAGUCACGG	7240	22028	C ₅ u ₅ C ₅ A ₅ u ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅			15994	Antisense
265	S27	UCCAUUAGCCCUAGUCACGGC	7241	22029	u ₅ C ₅ A ₅ u ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅			15995	Antisense
266	S27	CCAUCUAGCCCUAGUCACGGCU	7242	22030	C ₅ A ₅ A ₅ C ₅ u ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅ C ₅ u ₅ A ₅ g ₅			15996	Antisense

[illegible]

139	HCV+	GAGGCCAUAGUG	7278	22526	C ₅ A ₅ C ₅ U ₅ A ₅ U	CUGAUGAGGCCGUAAGGCCGAA	Icucuc B	16032	Inozyme
140	HCV+	AGAGCCAUAGUGG	7279	22527	C ₅ A ₅ A ₅ C ₅ U ₅ A	CUGAUGAGGCCGUAAGGCCGAA	Igcucu B	16033	Inozyme
281	HCV+	AAGGCCUUGUGGU	7280	22528	A ₅ C ₅ A ₅ A ₅ C ₅ A	CUGAUGAGGCCGUAAGGCCGAA	Igccuu B	16034	Inozyme
130	HCV+	CCCUCGCCGGAGA	7281	22529	U ₅ C ₅ U ₅ C ₅ C ₅ C	CUGAUGAGGCCGUAAGGCCGAA	Igaggg B	16035	Inozyme
280	HCV+	AAAGGCCUUGUGG	7282	22530	C ₅ A ₅ A ₅ C ₅ A	CUGAUGAGGCCGUAAGGCCGAA	Iccuuu B	16036	Inozyme
149	HCV+	GUGGUCUGCGGAA	7283	22531	U ₅ U ₅ C ₅ C ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Iaccac B	16037	Inozyme
194	HCV+	GGGUCUUCUUG	7284	22532	C ₅ A ₅ A ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Igaccc B	16038	Inozyme
255	HCV+	GCUAGCCGAGUAG	7285	22533	C ₅ U ₅ A ₅ C ₅ U	CUGAUGAGGCCGUAAGGCCGAA	Icuagc B	16039	Inozyme
294	HCV+	ACUGCCUGAUAGG	7286	22534	C ₅ A ₅ U ₅ A ₅ U	CUGAUGAGGCCGUAAGGCCGAA	Igcagu B	16040	Inozyme
293	HCV+	UACUGCCUGAUAG	7287	22535	C ₅ U ₅ A ₅ U ₅ C	CUGAUGAGGCCGUAAGGCCGAA	Icagua B	16041	Inozyme
290	HCV+	UGGUACUGCCUGA	7288	22536	U ₅ C ₅ A ₅ U ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Iuacca B	16042	Inozyme
169	HCV+	GUACACCGGAUU	7289	22537	A ₅ A ₅ U ₅ U ₅ CC	CUGAUGAGGCCGUAAGGCCGAA	Iuguac B	16043	Inozyme
293	HCV+	GUACUGCCUGAUAGG	7290	22544	C ₅ A ₅ U ₅ A ₅ U ₅ C	CUGAUGAGGCCGUAAGGCCGAA	Icaguac B	16044	Inozyme
294	HCV+	UACUGCCUGAUAGG	7291	22545	C ₅ A ₅ C ₅ U ₅ A	CUGAUGAGGCCGUAAGGCCGAA	Igcagua B	16045	Inozyme
281	HCV+	AAAGCCUUGUGGUA	7292	22546	U ₅ A ₅ C ₅ C ₅ A	CUGAUGAGGCCGUAAGGCCGAA	Igccuuu B	16046	Inozyme
166	HCV+	UGAGUACACCGGA	7293	22549	U ₅ A ₅ C ₅ U ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Ivacuca B	16047	Amberzyme
168	HCV+	AGUACACCGGAU	7294	22550	A ₅ U ₅ U ₅ C ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Uguacu B	16048	Amberzyme
141	HCV+	GAGCCAUAGUGGU	7295	22551	A ₅ C ₅ A ₅ U ₅ C	CUGAUGAGGCCGUAAGGCCGAA	Uggcuc B	16049	Amberzyme
156	HCV+	GCGGAACCGGUGA	7296	22552	U ₅ C ₅ A ₅ C ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Uuccgc B	16050	Amberzyme
155	HCV+	UGCGGAACCGGUG	7297	22553	C ₅ A ₅ C ₅ U ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Uccgca B	16051	Amberzyme
289	HCV+	GUGGUACUGCCUG	7298	22554	C ₅ A ₅ U ₅ U ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Uaccac B	16052	Amberzyme
297	HCV+	GCCUGAUAGGUG	7299	22555	C ₅ A ₅ C ₅ U ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Ucaggc B	16053	Amberzyme
166	HCV+	GUGAGUACACCGGAA	7300	22556	U ₅ U ₅ C ₅ C ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Uvacucac B	16054	Amberzyme
141	HCV+	AGAGCCAUAGUGGUC	7301	22557	G ₅ A ₅ C ₅ U ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Uggcucu B	16055	Amberzyme
156	HCV+	UGCGGAACCGGUGAG	7302	22558	C ₅ U ₅ C ₅ A ₅ U	CUGAUGAGGCCGUAAGGCCGAA	Uuccgca B	16056	Amberzyme
155	HCV+	CUGCGGAACCGGUGA	7303	22559	U ₅ C ₅ A ₅ C ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Uccgcag B	16057	Amberzyme
289	HCV+	UGUGGUACUGCCUGA	7304	22560	U ₅ C ₅ A ₅ U ₅ GC	CUGAUGAGGCCGUAAGGCCGAA	Uaccaca B	16058	Amberzyme
297	HCV+	UGCCUGAUAGGUGUC	7305	22561	G ₅ C ₅ A ₅ C ₅ U	CUGAUGAGGCCGUAAGGCCGAA	Ucaggca B	16059	Amberzyme
168	HCV+	GAGUACACCGGAUU	7306	22562	A ₅ A ₅ U ₅ U ₅ CC	CUGAUGAGGCCGUAAGGCCGAA	Uguacuac B	16060	Amberzyme
166	HCV-	UCCGGUGUACUCA	7307	22563	U ₅ G ₅ A ₅ U ₅ CC	gccgaaagGgagugaGguCu	accgga B	16061	Zinzyne
168	HCV-	AUUCGGUGUACU	7308	22564	A ₅ G ₅ U ₅ A ₅ C	gccgaaagGgagugaGguCu	cggaaau B	16062	Zinzyne
138	HCV-	ACUAUGGCUUCC	7309	22565	G ₅ G ₅ A ₅ U ₅ GC	gccgaaagGgagugaGguCu	cauagu B	16063	Zinzyne
156	HCV-	UCACCGGUUCCGC	7310	22566	G ₅ C ₅ U ₅ U ₅ GC	gccgaaagGgagugaGguCu	cgguga B	16064	Zinzyne
236	HCV-	GCGGGGACACGCC	7311	22567	G ₅ G ₅ C ₅ U ₅ GC	gccgaaagGgagugaGguCu	cccgcg B	16065	Zinzyne
279	HCV-	CACAAGGCCUUUC	7312	22568	G ₅ A ₅ A ₅ U ₅ GC	gccgaaagGgagugaGguCu	cuugug B	16066	Zinzyne

151	HCV-	GGUUCGCGAGACC	7313	22569	G ₅ G ₅ U ₅ C ₅ UG	gocgaaaggcgagugaGguGnu ggaacc B	16067	Zinzyme
292	HCV-	UAUCAGGCAGUAC	7314	22570	G ₅ U ₅ A ₅ C ₅ UG	gocgaaaggcgagugaGguGnu cugaua B	16068	Zinzyme
289	HCV-	CAGGCAGUACCCAC	7315	22571	G ₅ U ₅ G ₅ G ₅ UA	gocgaaaggcgagugaGguGnu ugccug B	16069	Zinzyme
166	HCV-	UUCCGGUGUACUCAC	7316	22572	G ₅ U ₅ G ₅ A ₅ GUA	gocgaaaggcgagugaGguGnu accggaa B	16070	Zinzyme
279	HCV-	CCACAAGGCCUUUCG	7317	22573	C ₅ G ₅ A ₅ A ₅ AGG	gocgaaaggcgagugaGguGnu cuuuggg B	16071	Zinzyme
156	HCV-	CUCACGGUUCGCCA	7318	22574	U ₅ G ₅ C ₅ G ₅ GA	gocgaaaggcgagugaGguGnu cggugag B	16072	Zinzyme
138	HCV-	CACUAUGGCUCUCC	7319	22575	G ₅ G ₅ G ₅ A ₅ GA	gocgaaaggcgagugaGguGnu caugag B	16073	Zinzyme
151	HCV-	CGGUUCGCGAGACCA	7320	22576	U ₅ G ₅ G ₅ U ₅ CUG	gocgaaaggcgagugaGguGnu ggaaccg B	16074	Zinzyme
292	HCV-	CUAUCAGGCAGUACC	7321	22577	G ₅ G ₅ U ₅ A ₅ CUG	gocgaaaggcgagugaGguGnu cugauag B	16075	Zinzyme
289	HCV-	UCAGGCAGUACCCACA	7322	22578	U ₅ G ₅ U ₅ G ₅ GUA	gocgaaaggcgagugaGguGnu ugccuga B	16076	Zinzyme
168	HCV-	AAUUCGGUGUACUC	7323	22579	G ₅ A ₅ G ₅ U ₅ ACA	gocgaaaggcgagugaGguGnu cggaauu B	16077	Zinzyme
163	HCV-	GGUGUACUCACCG	7324	22580	C ₅ G ₅ G ₅ U ₅ GA	CUGAUGagggccgguuagggccGaa Uacacc B	16078	Amberzyme
159	HCV-	UACUCACCGGUUC	7325	22581	G ₅ A ₅ A ₅ C ₅ CG	CUGAUGagggccgguuagggccGaa Uaguaa B	16079	Amberzyme
140	HCV-	CCACUAUGGCUCU	7326	22582	A ₅ G ₅ A ₅ G ₅ CC	CUGAUGagggccgguuagggccGaa Uagugg B	16080	Amberzyme
281	HCV-	ACCACAAGGCCUU	7327	22583	A ₅ A ₅ G ₅ G ₅ CC	CUGAUGagggccgguuagggccGaa Uguugu B	16081	Amberzyme
233	HCV-	GGGCACGCCCAA	7328	22584	U ₅ U ₅ G ₅ G ₅ GC	CUGAUGagggccgguuagggccGaa Ugcccc B	16082	Amberzyme
143	HCV-	AGACCACUAUGGC	7329	22585	G ₅ C ₅ C ₅ A ₅ UA	CUGAUGagggccgguuagggccGaa Uggucu B	16083	Amberzyme
146	HCV-	CGCAGACCACUAU	7330	22586	A ₅ U ₅ A ₅ G ₅ UG	CUGAUGagggccgguuagggccGaa Ucugcg B	16084	Amberzyme
195	HCV-	CCAAAGAAAGGACC	7331	22587	G ₅ G ₅ U ₅ C ₅ CU	CUGAUGagggccgguuagggccGaa Ucuugg B	16085	Amberzyme
194	HCV-	CAAGAAAGGACCC	7332	22588	G ₅ G ₅ G ₅ U ₅ CC	CUGAUGagggccgguuagggccGaa Ucuuug B	16086	Amberzyme
283	HCV-	GUACCACAAGGCC	7333	22589	G ₅ G ₅ C ₅ C ₅ UU	CUGAUGagggccgguuagggccGaa Ugguaa B	16087	Amberzyme
286	HCV-	GCAGUACCAACAG	7334	22590	C ₅ U ₅ U ₅ G ₅ UG	CUGAUGagggccgguuagggccGaa Uacugc B	16088	Amberzyme
296	HCV-	ACCUCUACAGGCA	7335	22591	U ₅ G ₅ C ₅ C ₅ UG	CUGAUGagggccgguuagggccGaa Uagggg B	16089	Amberzyme
190	HCV-	AAAGGACCCGGUC	7336	22592	G ₅ A ₅ C ₅ C ₅ GG	CUGAUGagggccgguuagggccGaa Uccuuu B	16090	Amberzyme
163	HCV-	CGGUGUACUCACCGG	7337	22593	C ₅ C ₅ G ₅ G ₅ UGA	CUGAUGagggccgguuagggccGaa Uacaccg B	16091	Amberzyme
140	HCV-	ACCACUAUGGUCUC	7338	22594	G ₅ A ₅ G ₅ A ₅ GCC	CUGAUGagggccgguuagggccGaa Uaguggu B	16092	Amberzyme
159	HCV-	GUACUCACCGGUUCC	7339	22595	G ₅ G ₅ A ₅ A ₅ CCG	CUGAUGagggccgguuagggccGaa Uaguuac B	16093	Amberzyme
233	HCV-	GGGGCACGCCCAAA	7340	22596	U ₅ U ₅ U ₅ G ₅ GGC	CUGAUGagggccgguuagggccGaa Ugccccc B	16094	Amberzyme
143	HCV-	CAGACCACUAUGGU	7341	22597	A ₅ G ₅ C ₅ C ₅ AUA	CUGAUGagggccgguuagggccGaa Uggucug B	16095	Amberzyme
146	HCV-	CCGCAGACCACUAUG	7342	22598	C ₅ A ₅ U ₅ A ₅ GUG	CUGAUGagggccgguuagggccGaa Ucugcgg B	16096	Amberzyme
195	HCV-	UCCAAGAAAGGACCC	7343	22599	G ₅ G ₅ G ₅ U ₅ CCU	CUGAUGagggccgguuagggccGaa Ucuugga B	16097	Amberzyme
283	HCV-	AGUACCACAAGGCCU	7344	22600	A ₅ G ₅ G ₅ C ₅ CUU	CUGAUGagggccgguuagggccGaa Ugguaa B	16098	Amberzyme
281	HCV-	UACCACAAGGCCUUU	7345	22601	A ₅ A ₅ A ₅ G ₅ GCC	CUGAUGagggccgguuagggccGaa Uguuggu B	16099	Amberzyme
296	HCV-	CACCCUAUCAGGCAG	7346	22602	C ₅ U ₅ G ₅ C ₅ CUG	CUGAUGagggccgguuagggccGaa Uagggug B	16100	Amberzyme
286	HCV-	GGCAGUACCACAAGG	7347	22603	C ₅ C ₅ U ₅ U ₅ GUG	CUGAUGagggccgguuagggccGaa Uacugcc B	16101	Amberzyme

7985	HCV-	UCUCAGU G UCUCUCA	7348	22719	uggaaga uGAUg gcaUGcacuaugc gCg acugaga B	16102	G-cleaver
4832	HCV-	UGUAUAI G CCUCUCC	7349	22720	ggagagg uGAUg gcaUGcacuaugc gCg auauaca B	16103	G-cleaver
4153	HCV-	ACCGUGU G CCUUAAG	7350	22721	ucuaagg uGAUg gcaUGcacuaugc gCg acacggg B	16104	G-cleaver
3200	HCV-	GUGGAGU G AGGUGGU	7351	22722	accaccu uGAUg gcaUGcacuaugc gCg acuccac B	16105	G-cleaver
1682	HCV-	ACGAGUU G AACCUGU	7352	22723	acagguu uGAUg gcaUGcacuaugc gCg aacucgu B	16106	G-cleaver
896	HCV+	CCUGUCU G ACCAUCC	7353	22724	ggauggu uGAUg gcaUGcacuaugc gCg agacagg B	16107	G-cleaver
2504	HCV+	UCCUGUU G CUUUUCC	7354	22725	ggaaaag uGAUg gcaUGcacuaugc gCg aacagga B	16108	G-cleaver
2651	HCV+	UCCUGUU G UCUUUCU	7355	22726	agaagaa uGAUg gcaUGcacuaugc gCg acagga B	16109	G-cleaver
4094	HCV+	ACAAAGU G CUCGUCC	7356	22727	ggacggg uGAUg gcaUGcacuaugc gCg acuuugu B	16110	G-cleaver
8970	HCV+	GCCACUU G ACCUACC	7357	22728	gguaggu uGAUg gcaUGcacuaugc gCg aaguggc B	16111	G-cleaver
1200	HCV+	CUUCCUC G UCUCUCA	7358	22747	ugagaga gccgaaggCGagugagGGuCu gaggaag B	16112	Zinzyme
1211	HCV+	CUCAGCU G UUCACCU	7359	22748	aggucaa gccgaaggCGagugagGGuCu agcugag B	16113	Zinzyme
2504	HCV+	UCCUGUU G CUUUUCC	7354	22749	ggaaaag gccgaaggCGagugagGGuCu aacagga B	16114	Zinzyme
2651	HCV+	UCCUGUU G UCUUUCU	7355	22750	agaagaa gccgaaggCGagugagGGuCu acgagga B	16115	Zinzyme
8811	HCV+	CACUCCA G UCUUUCU	7360	22751	gaguuga gccgaaggCGagugagGGuCu uggagug B	16116	Zinzyme
8594	HCV-	UCGCCGC G UCCUCUU	7361	22752	aagagga gccgaaggCGagugagGGuCu gcggcga B	16117	Zinzyme
7985	HCV-	UCUCAGU G UCUCUCA	7348	22753	uggaaga gccgaaggCGagugagGGuCu acugaga B	16118	Zinzyme
6611	HCV-	CUUCCAC G UACUCCU	7362	22754	aggagua gccgaaggCGagugagGGuCu guggagg B	16119	Zinzyme
5631	HCV-	UCCACAU G UGUUUCG	7363	22755	cgaagca gccgaaggCGagugagGGuCu augugga B	16120	Zinzyme
821	HCV-	UCACGCC G UCUUCCA	7364	22756	uggaaga gccgaaggCGagugagGGuCu ggcguga B	16121	Zinzyme
870	HCV+	CUCUAUC U UCCUCUU	7365	22775	aagagga CUGAUGAgccguuaggccGAA Iauagga B	16122	Inozyme
1210	HCV+	UCUCAGC U GUUCACC	7366	22776	ggugaac CUGAUGAgccguuaggccGAA Icuagga B	16123	Inozyme
2642	HCV+	UCCUCUC C UUCUUCG	7367	22777	cgaggaa CUGAUGAgccguuaggccGAA Iagagga B	16124	Inozyme
5726	HCV+	UCACAGC C UCCAUCA	7368	22778	ugaugga CUGAUGAgccguuaggccGAA Icuugga B	16125	Inozyme
8142	HCV+	UCCACC C UUCUCA	7369	22779	ugaggaa CUGAUGAgccguuaggccGAA Iguaggag B	16126	Inozyme
7990	HCV-	UGGUGUC U CAGUGUC	7370	22780	gacacug CUGAUGAgccguuaggccGAA Iacacca B	16127	Inozyme
7813	HCV-	UUCGCC U UCAUCUC	7371	22781	gagagga CUGAUGAgccguuaggccGAA Igcgaag B	16128	Inozyme
7137	HCV-	ACCUCUC U CUCAUCC	7372	22782	ggaugag CUGAUGAgccguuaggccGAA Iagaggu B	16129	Inozyme
6084	HCV-	UUAUCC A CUGACA	7373	22783	uguugag CUGAUGAgccguuaggccGAA Igaugaa B	16130	Inozyme
2554	HCV-	CAACAGC A UCAUCCA	7374	22784	uggaaga CUGAUGAgccguuaggccGAA Icuugug B	16131	Inozyme
1202	HCV+	UCCUGU C UCUCAGC	7375	22943	gcugaga CUGAUGAgccguuaggccGAA Agagga B	16132	Hammerhead
1607	HCV+	GGCACAU U AACAGGA	7376	22944	uccuguu CUGAUGAgccguuaggccGAA Augugcc B	16133	Hammerhead
2639	HCV+	GCAUCU C UCCUUCU	7377	22945	ggaagga CUGAUGAgccguuaggccGAA Aggaugc B	16134	Hammerhead
6610	HCV+	GAGGAGU A CGUGGAG	7378	22946	cuccacg CUGAUGAgccguuaggccGAA Acuccuc B	16135	Hammerhead
9014	HCV+	GGGCAU U UCACUCC	7379	22947	ggaguga CUGAUGAgccguuaggccGAA Aaugcgc B	16136	Hammerhead
8605	HCV-	GACUUGU A GGUUGGC	7380	22948	gcgagcc CUGAUGAgccguuaggccGAA Acgaguc B	16137	Hammerhead
7983	HCV-	UCAGUGU C UUCACGC	7381	22949	gcuggaa CUGAUGAgccguuaggccGAA Acacuga B	16138	Hammerhead
7136	HCV-	CCUCCU C UCAUCCU	7382	22950	aggaaga CUGAUGAgccguuaggccGAA Agagagg B	16139	Hammerhead
6609	HCV-	UCCACU A UCCUCA	7383	22951	ugaggag CUGAUGAgccguuaggccGAA Acgugga B	16140	Hammerhead
6292	HCV-	CGUGCAU A UCCAGUC	7384	22952	gacugga CUGAUGAgccguuaggccGAA Augcacg B	16141	Hammerhead
867	HCV+	UUUCU C A UCUCUCC	7385	22971	aggaaga GCCTAGCTACAACGA agagaaa B	16142	DNAzyme
1200	HCV+	CUUCCUC G UCUCUCA	7358	22972	ugagaga GCCTAGCTACAACGA gaggaag B	16143	DNAzyme
1211	HCV+	CUCAGCU G UUCACCU	7359	22973	aggugaa GCCTAGCTACAACGA agcugag B	16144	DNAzyme
5730	HCV+	AGCCUCC A UCACAG	7386	22974	cugguga GCCTAGCTACAACGA ggaggcu B	16145	DNAzyme
6533	HCV+	UCAAGGC A UACACCA	7387	22975	uggugua GCCTAGCTACAACGA gcguuga B	16146	DNAzyme

8594	HCV-	UCGCCGC G UCCUCUU	7361	22976	aagagga GGCTAGCTACAACGA ggggcga B	16147	DNAzyme
7810	HCV-	CGCCUUC A UCUCUU	7388	22977	aagagga GGCTAGCTACAACGA gaagcgc B	16148	DNAzyme
7133	HCV-	CUCUC A UCUCUU	7389	22978	aggagga GGCTAGCTACAACGA gagagag B	16149	DNAzyme
6611	HCV-	CCUCCAC G UACUCCU	7362	22979	aggagua GGCTAGCTACAACGA guggagg B	16150	DNAzyme
2300	HCV-	CCUCCAA A UCACAA	7390	22980	guuguga GGCTAGCTACAACGA uuggagg B	16151	DNAzyme
195	HCV+	GGGUCCU U UCUUGGA	7148	23072	c _g c _g a _g a _g ga cUGAuGaggcgWWagccGaa Aggacc B	16152	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	23076	WWWWC _B c _g a _g a _g ga cUGAuGaggcguuagccGaa Aggacc B	16153	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	23077	WWWC _g c _g a _g a _g ga cUGAuGaggcgWWagccGaa Aggacc B	16154	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	23086	c _g c _g a _g a _g ga cUGAuGaggcgWWagccGaa Aggacc B	16155	Hammerhead

lower case = 2'-O-methyl

UPPER CASE = RIBO

B = inverted deoxy abasic

U = 2'-deoxy-2'-amino Uridine

C = 2'-deoxy-2'-amino Cytidine

U = 2'-deoxy-2'-amino Uridine

Z = BRdU (5-bromo-2'-deoxy Uridine)

W = acyclic galactose-amine linker

UNDERLINE = deoxy nucleotide

TABLE XXI: ANTI HCV AMINO CONTAINING HAMMERHEAD RIBOZYME AND CONTROL SEQUENCES

pos	RPI#	HCV 5'UTR Site	Ribozyme Sequences (5'-3')	Core	Rz Seq ID
62	12257	HCV-62	g _s c _s g _s ugaa cUGAUGaggccguuaggccGaa AcaguagB	Active	15897
79	12258	HCV-79	a _s u _s g _s gcua cUGAUGaggccguuaggccGaa AcgcuuB	Active	15898
81	12249	HCV-81	c _s c _s a _s uggc cUGAUGaggccguuaggccGaa AgacguB	Active	15899
104	12259	HCV-104	g _s c _s u _s gcac cUGAUGaggccguuaggccGaa AcacuaB	Active	15900
142	12250	HCV-142	a _s g _s a _s ccac cUGAUGaggccguuaggccGaa AuggcucB	Active	15901
148	12251	HCV-148	u _s u _s c _s cgca cUGAUGaggccguuaggccGaa AccacuaB	Active	15902
165	12260	HCV-165	u _s c _s c _s ggug cUGAUGaggccguuaggccGaa AcucaccB	Active	15903
192	12261	HCV-192	a _s a _s g _s aaag cUGAUGaggccguuaggccGaa AcccgguB	Active	15904
195	12252	HCV-195	u _s c _s c _s aaaga cUGAUGaggccguuaggccGaa AggaccB	Active	15905
196	12262	HCV-196	a _s u _s c _s caag cUGAUGaggccguuaggccGaa AaggaccB	Active	15906
270	12263	HCV-270	c _s u _s u _s ucgc cUGAUGaggccguuaggccGaa AcccaacB	Active	15907
282	12264	HCV-282	g _s u _s a _s ccac cUGAUGaggccguuaggccGaa AggccuB	Active	15908
306	12265	HCV-306	c _s a _s c _s ucgc cUGAUGaggccguuaggccGaa AgcaccB	Active	15909
325	12253	HCV-325	u _s c _s u _s acga cUGAUGaggccguuaggccGaa AccuccB	Active	15910
330	12254	HCV-330	c _s a _s c _s gguc cUGAUGaggccguuaggccGaa AcgagacB	Active	15911
Control Sequences					
79	13274	HCV-79 AC2	c _s u _s u _s aggu cUAGUGaggccguuaggccGau AguucucB	Attenuated	16171
81	13271	HCV-81 AC	u _s c _s u _s gccg cUAGUGaggccguuaggccGau AgugaccB	Attenuated	16172
142	13270	HCV-142 AC	a _s a _s c _s ccug cUAGUGaggccguuaggccGau AgcucguB	Attenuated	16173
192	13272	HCV-192 AC	a _s g _s u _s agaa cUAGUGaggccguuaggccGau AgcugccB	Attenuated	16174
195	13269	HCV-195 AC	g _s a _s u _s ucca cUAGUGaggccguuaggccGau AcgcgacB	Attenuated	16175
282	13273	HCV-282 AC	g _s c _s c _s auuc cUAGUGaggccguuaggccGau AucuggcB	Attenuated	16176
330	13268	HCV-330 AC	c _s c _s a _s ggcu cUAGUGaggccguuaggccGau AaugcgB	Attenuated	16177
195	15291	HCV-195 BAC3	u _s c _s c _s aaaga cUAGUGacgccguuaggcgGaa AggaccB	Attenuated	16178
195	15292	HCV-195 SAC3	a _s g _s a _s cuac cUAGUGacgccguuaggcgGaa AcccgagB	Attenuated	16179
330	15294	HCV-330 BAC	c _s a _s c _s gguc cUAGUGacgccguuaggcgGaa AcgagacB	Attenuated	16180
330	15295	HCV-330 SAC	g _s c _s u _s ccga cUAGUGacgccguuaggcgGaa AgacacB	Attenuated	16181

UPPER CASE = RIBO; lower case = 2'-O-methyl; B = inverted deoxyabasic;

s = phosphorothioate linkage

U = 2'-deoxy-2'-amino uridine

**TABLE XXII: ANTI HCV SITE 330 ANTISENSE NUCLEIC ACID AND
SCRAMBLED CONTROL SEQUENCES**

pos	RPI #	Alias	Antisense Nucleic Acid	Seq ID #
330	17501	HCV.5-330 antisense	G _S T _S G _S C _S T _S C _S A _S T _S G _S A _S T _S G _S C _S A _S C _S G _S G _S T _S C _S T	15898
330	17498	HCV.5-330 antisense	G _S T _S G _S C _S T _S C _S A _S T _S G _S G _S T _S G _S C _S A _S C _S G _S G _S T _S C _S T	16182

pos	RPI#	Alias	Control Sequence	Seq ID #
330	17499	HCV.5-330 scrambled	T _S G _S A _S T _S C _S A _S G _S G _S T _S C _S T _S G _S C _S T _S G _S C _S G _S T _S G _S C	16183
330	17502	HCV.5-330 Scrambled	T _S G _S A _S T _S C _S A _S G _S G _S T _S C _S T _S G _S C _S T _S G _S C _S A _S T _S G _S C	16184

UPPER CASE = Deoxy Nucleotide
s = phosphorothioate

TABLE XXIII: IN VITRO CLEAVAGE DATA, ANTI-HCV ENZYMATIC NUCLEIC ACIDS

Seq ID #	RPI#	Motif	Site (+/-)	Enzymatic Nucleic Acid Sequence	% Substrate Cleaved in 3 hours	Substrate Sequence	Seq ID #	Substrate RPI#
16132	22943	Hammerhead	1190 (+)	gugaga CUGAUGAggcccguuaggccGAA Acgagga B	89.57	UCCUCGU C UCUCAGC B	7391	22897
16133	22944	Hammerhead	1595 (+)	uccuguu CUGAUGAggcccguuaggccGAA Augugcc B	90.33	GGCACAU U AACAGGA B	7392	22898
16134	22945	Hammerhead	2627 (+)	ggaagga CUGAUGAggcccguuaggccGAA Aggaugc B	82.54	GCAUCCU C UCCUCC B	7393	22899
16135	22946	Hammerhead	6598 (+)	cuccacg CUGAUGAggcccguuaggccGAA Acuccuc B	78.06	GAGGAGU A CGUGGAG B	7394	22900
16136	22947	Hammerhead	9002 (+)	ggaguga CUGAUGAggcccguuaggccGAA Auugocg B	81.88	GCGCAUU U UCACUCC B	7395	22901
16137	22948	Hammerhead	818 (-)	gcagoc CUGAUGAggcccguuaggccGAA Acgaguc B	88.34	GACUCGU A GGCUCGC B	7396	22902
16138	22949	Hammerhead	1440 (-)	gcuggaa CUGAUGAggcccguuaggccGAA Acacuga B	89.16	UCAGUGU C UCCAGC B	7397	22903
16139	22950	Hammerhead	2287 (-)	aggaua CUGAUGAggcccguuaggccGAA Agagagg B	83.43	CCUCUCU C UCAUCCU B	7398	22904
16140	22951	Hammerhead	2814 (-)	ugaggag CUGAUGAggcccguuaggccGAA Acgugga B	83.25	UCCACGU A CUCCUCA B	7399	22905
16141	22952	Hammerhead	3131 (-)	gacugga CUGAUGAggcccguuaggccGAA Augcaog B	86.96	CGUGCAU A UCCAGUC B	7400	22906
16142	22971	DNAzyme	855 (+)	aggaaga GGCTAGCTAGCAACGA agagaaa B	92.11	UUUCUCU A UCUCUCC B	7401	22925
16143	22972	DNAzyme	1188 (+)	ugagaga GGCTAGCTAGCAACGA gaggaag B	86.38	CUUCCUC G UCUCUCA B	7402	22926
16144	22973	DNAzyme	1199 (+)	aggugaa GGCTAGCTAGCAACGA agcugag B	83.15	CUCAGCU G UUCACCU B	7403	22927
16145	22974	DNAzyme	5718 (+)	cugguga GGCTAGCTAGCAACGA ggaggcu B	57.82	AGCCUCC A UACCCAG B	7404	22928
16146	22975	DNAzyme	6521 (+)	uggugua GGCTAGCTAGCAACGA gcuuga B	75.77	UCAAAGC A UACACCA B	7405	22929
16147	22976	DNAzyme	829 (-)	aaggaga GGCTAGCTAGCAACGA geggaga B	66.06	UCGCCGC G UCCUCUU B	7406	22930
16148	22977	DNAzyme	1613 (-)	aaggaga GGCTAGCTAGCAACGA gaaggcg B	71.28	CGCCUUC A UCUCUUU B	7407	22931
16149	22978	DNAzyme	2290 (-)	aggagga GGCTAGCTAGCAACGA gegagag B	61.60	CUCUCUC A UCCUCCU B	7408	22932
16150	22979	DNAzyme	2812 (-)	aggagua GGCTAGCTAGCAACGA guggagg B	85.53	CCUCCAC G UACUCCU B	7409	22933
16151	22980	DNAzyme	7123 (-)	guuguga GGCTAGCTAGCAACGA uuggagg B	34.60	CCUCCAA A UCAGAAC B	7410	22934
16102	22719	G-cleaver	1438 (+)	uggaaga uGAUg gcauGcaciaugc gCg acugaga B	69.88	UCUCAGU G UCUCUCA B	7411	22813
16103	22720	G-cleaver	4591 (+)	ggagagg uGAUg gcauGcaciaugc gCg auauaca B	77.74	UGUAUUAU G CCUCUCC B	7412	22814
16104	22721	G-cleaver	5270 (+)	ucuaagg uGAUg gcauGcaciaugc gCg acacggg B	47.37	ACCGUGU G CCUUAGA B	7413	22815
16105	22722	G-cleaver	6223 (+)	accacuu uGAUg gcauGcaciaugc gCg acuccac B	75.84	GUGGAGU G AGGUGGU B	7414	22816
16106	22723	G-cleaver	7741 (+)	acagguu uGAUg gcauGcaciaugc gCg aacucgu B	61.58	ACGAGUU G AACCUGU B	7415	22817
16107	22724	G-cleaver	884 (-)	ggauggu uGAUg gcauGcaciaugc gCg agacagg B	65.16	CCUGUCU G ACCAUCC B	7416	22818
16108	22725	G-cleaver	2492 (-)	ggaaag uGAUg gcauGcaciaugc gCg aacagga B	94.66	UCCUGUU G CUUUUCC B	7417	22819
16109	22726	G-cleaver	2639 (-)	agaagaa uGAUg gcauGcaciaugc gCg acgagga B	82.14	UCCUCGU G UUCUUUCU B	7418	22820

16110	22727	G-cleaver	4082 (-)	ggacgag uGAUg gcaUGcacaugc gCg acuuugu B	67.20	ACAAAGU G CUCGUCC B	7419	22821
16111	22728	G-cleaver	8958 (-)	gguaugu uGAUg gcaUGcacaugc gCg aaguggc B	81.06	GCCACUU G ACCUAGC B	7420	22822
16112	22747	Zinzyme	1188 (+)	ugagaga gccgaaggGgagugaGGuCu gaggaa B	66.11	CUUCCUC G UCUCUCA B	7402	22841
16113	22748	Zinzyme	1199 (+)	aggugaa gccgaaggGgagugaGGuCu agcugag B	80.28	CUCAGCU G UUCACCU B	7403	22842
16114	22749	Zinzyme	2492 (+)	ggaaaag gccgaaggGgagugaGGuCu aacagga B	90.80	UCCUGUU G CUUUUCC B	7417	22843
16115	22750	Zinzyme	2639 (+)	agaagaa gccgaaggGgagugaGGuCu acagga B	80.64	UCCUCGU G UUCUUCU B	7418	22844
16116	22751	Zinzyme	8799 (+)	gaguuga gccgaaggGgagugaGGuCu ugagag B	14.85	CACUCCA G UCAACUC B	7421	22845
16117	22752	Zinzyme	829 (-)	aagagga gccgaaggGgagugaGGuCu gccgga B	27.83	UGGCCGC G UCCUCUU B	7406	22846
16118	22753	Zinzyme	1438 (-)	uggaaga gccgaaggGgagugaGGuCu acugaga B	89.39	UCUCAGU G UCUUCCA B	7411	22847
16119	22754	Zinzyme	2812 (-)	aggagua gccgaaggGgagugaGGuCu guggagg B	50.40	CCUCCAC G UACUCCU B	7409	22848
16120	22755	Zinzyme	3790 (-)	cgaagca gccgaaggGgagugaGGuCu augugga B	81.10	UCCACAU G UGCUUCG B	7422	22849
16121	22756	Zinzyme	8602 (-)	uggaaga gccgaaggGgagugaGGuCu ggcguga B	73.47	UCACGCC G UCUUCCA B	7423	22850
16122	22775	Inozyme	858 (+)	aagagga CUGAUGAggcccguuaggccGAA laugag B	87.74	CUCUAUC U UCCUCUU B	7424	22869
16123	22776	Inozyme	1198 (+)	gguaaac CUGAUGAggcccguuaggccGAA lcugaga B	84.55	UCUCAGC U GUUCACC B	7425	22870
16124	22777	Inozyme	2630 (+)	cgaggaa CUGAUGAggcccguuaggccGAA lagagga B	90.12	UCCUCUC C UUCUUCG B	7426	22871
16125	22778	Inozyme	5714 (+)	ugaagga CUGAUGAggcccguuaggccGAA lcuguga B	83.77	UCACAGC C UCCAUCA B	7427	22872
16126	22779	Inozyme	8130 (+)	ugaggaa CUGAUGAggcccguuaggccGAA lguggag B	82.22	CUCCACC C UCCUCA B	7428	22873
16127	22780	Inozyme	1433 (-)	gacacug CUGAUGAggcccguuaggccGAA lacacca B	87.33	UGGUGUC U CAGUGUC B	7429	22874
16128	22781	Inozyme	1610 (-)	gagauga CUGAUGAggcccguuaggccGAA lgcgaag B	70.67	CUUCGCC U UCAUCUC B	7430	22875
16129	22782	Inozyme	2286 (-)	ggaugag CUGAUGAggcccguuaggccGAA lagaggu B	78.83	ACCUCUC U CUCAUCC B	7431	22876
16130	22783	Inozyme	3339 (-)	ugugcag CUGAUGAggcccguuaggccGAA lgaugaa B	86.93	UUCAUCC A CUGCACA B	7432	22877
16131	22784	Inozyme	6869 (-)	uggauga CUGAUGAggcccguuaggccGAA lcugug B	90.41	CAACAGC A UCAUCCA B	7433	22878

In vitro cleavage in 50 mM Tris-Cl, pH 8.0, 40 mM Mg²⁺ at 37°, using trace substrate, and enzymatic nucleic acid concentration of 500 nM or greater.

UPPER CASE = RIBO

UNDERLINED = DEOXY

lower case = 2'-O-methyl

B = inverted deoxybasic

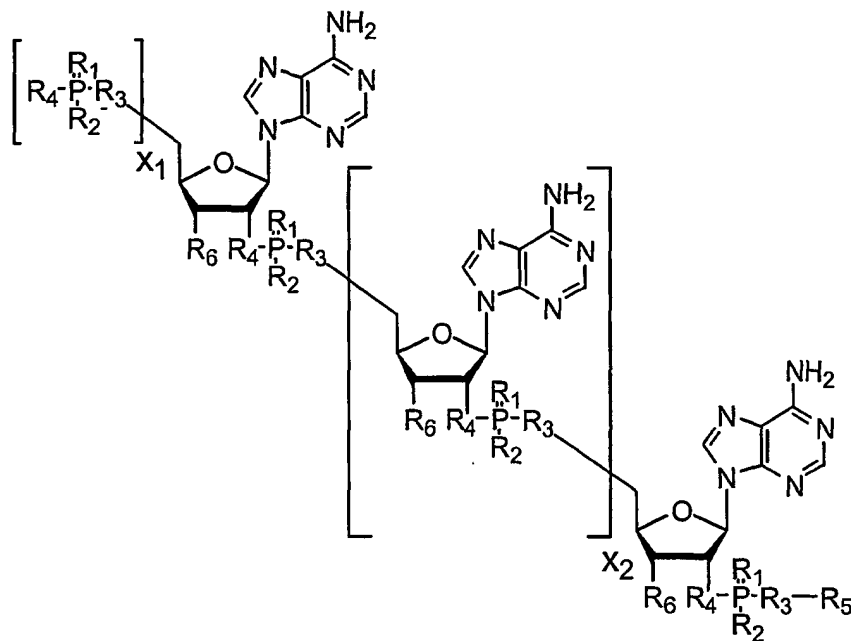
C = 2'-amino C

(+/-) = plus strand/minus strand of HCV genome

CLAIMS

What we claim is:

1. A compound having Formula I:



- 5 wherein X₁ is an integer selected from the group consisting of 1, 2, and 3; X₂ is an integer greater than or equal to 1; R₆ is independently selected from the group consisting of H, OH, NH₂, O NH₂, alkyl, S-alkyl, O-alkyl, O-alkyl-S-alkyl, O-alkoxyalkyl, allyl, O-allyl, and fluoro; each R₁ and R₂ are independently selected from the group consisting of O and S; each R₃ and R₄ are independently selected from the group consisting of O, N, and S; and R₅
- 10 is selected from the group consisting of alkyl, alkylamine, oligonucleotide having any of SEQ ID NOS. 11343-16182, oligonucleotide having a sequence complementary to any of SEQ ID NOS. 2594-7433, and abasic moiety.
2. The compound of claim 1, wherein said oligonucleotide having a sequence complementary to any of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid molecule.
- 15 3. The compound of claim 1, wherein said oligonucleotide having a sequence complementary to any of SEQ ID NOS. 2594-7433 is an antisense nucleic acid molecule.

4. The compound of claim 2, wherein said enzymatic nucleic acid molecule is selected from the group consisting of Hammerhead, Inozyme, G-cleaver, DNAzyme, Amberzyme, and Zinzyme motifs.
5. The compound of claim 2, wherein said Inozyme enzymatic nucleic acid molecule comprises a stem II region of length greater than or equal to 2 base pairs.
6. The compound of claim 2, wherein said enzymatic nucleic acid comprises between 12 and 100 bases complementary to an RNA derived from HCV.
7. The compound of claim 2, wherein said enzymatic nucleic acid comprises between 14 and 24 bases complementary to an RNA derived from HCV.
8. The compound of claim 3, wherein said antisense nucleic acid comprises between 12 and 100 bases complementary to an RNA derived from HCV.
9. The compound of claim 3, wherein said antisense nucleic acid comprises between 14 and 24 bases complementary to an RNA derived from HCV.
10. A composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier.
11. A mammalian cell comprising a compound of claim 1.
12. The mammalian cell of claim 11, wherein said mammalian cell is a human cell.
13. A method for treatment of cirrhosis, liver failure, hepatocellular carcinoma, or a condition associated with HCV infection comprising the step of administering to a patient a compound of claim 1 under conditions suitable for said treatment.
14. The method of claim 13 further comprising the use of one or more drug therapies under conditions suitable for said treatment.
15. A method for inhibiting HCV replication in a mammalian cell comprising the step of administering to said cell the compound of claim 1 under conditions suitable for said inhibition.

16. A method of cleaving a separate RNA molecule comprising contacting the compound of claim 1 with said separate RNA molecule under conditions suitable for the cleavage of said separate RNA molecule.
17. The method of claim 16, wherein said cleavage is carried out in the presence of a divalent
5 cation.
18. The method of claim 17, wherein said divalent cation is Mg^{2+} .
19. The method of claim 16, wherein said cleavage is carried out in the presence of a protein nuclease.
20. The method of claim 19, wherein said protein nuclease is an RNase L.
- 10 21. The compound of claim 1, wherein said compound is chemically synthesized.
22. The compound of claim 1, wherein said oligonucleotide comprises at least one 2'-sugar modification.
23. The compound of claim 1, wherein said oligonucleotide comprises at least one nucleic acid base modification.
- 15 24. The compound of claim 1, wherein said oligonucleotide comprises at least one phosphate modification.
25. The method of claim 14, wherein said drug therapy is the administration of type I interferon.
26. The method of claim 25, wherein said type I interferon and the compound of claim 1 are administered simultaneously.
- 20 27. The method of claim 25, wherein said type I interferon and the compound of claim 1 are administered separately.
28. The method of claim 25, wherein said type I interferon is selected from the group consisting of interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon,

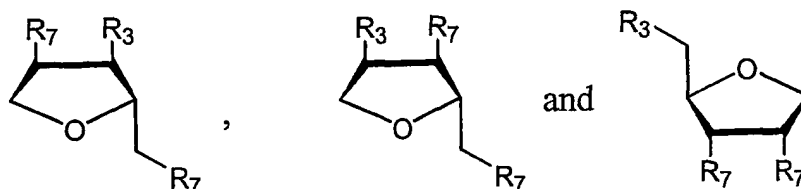
polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, and polyethylene glycol consensus interferon.

29. The method of claim 14, wherein R₅ in said compound is selected from the group consisting of alkyl, alkylamine and abasic moiety and said drug therapy comprises treatment with an enzymatic nucleic acid molecule which is targeted against HCV replication.

30. The method of claim 14, wherein R₅ in said compound is selected from the group consisting of alkyl, alkylamine and abasic moiety and said drug therapy comprises treatment with an antisense nucleic acid molecule which is targeted against HCV replication.

31. A composition comprising type I interferon and the compound of claim 1 and a pharmaceutically acceptable carrier.

32. The compound of claim 1, wherein said abasic moiety is selected from the group consisting of:



wherein R₃ is selected from the group consisting of S, N, or O and R₇ is independently selected from the group consisting of H, OH, NH₂, O-NH₂, alkyl, S-alkyl, O-alkyl, O-alkyl-S-alkyl, O-alkoxyalkyl, allyl, O-allyl, fluoro, oligonucleotide, alkyl, alkylamine and abasic moiety.

33. An enzymatic nucleic acid molecule that specifically cleaves RNA derived from hepatitis B virus (HBV), wherein said enzymatic nucleic acid molecule comprises sequence defined as Seq. ID No. 6346.

34. A method of administering to a cell an enzymatic nucleic acid molecule of claim 33 comprising contacting said cell with the enzymatic nucleic acid molecule under conditions suitable for said administration.

35. The method of claim 34, further comprising the administration of one or more other therapeutic compounds.
36. The method of claim 35, wherein said other therapeutic compound is type I interferon.
37. The method of claim 35, wherein said other therapeutic compound is 3TC® (Lamivudine).
- 5 38. The method of claim 35, wherein said other therapeutic compound and the enzymatic nucleic acid molecule are administered simultaneously.
39. The method of claim 35, wherein said other therapeutic compound and enzymatic nucleic acid molecule are administered separately.
- 10 40. The method of claim 36, wherein said type I interferon is selected from the group consisting of interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, and polyethylene glycol consensus interferon.
41. The method of claim 34 or claim 35, wherein said cell is a mammalian cell.
42. The method of claim 41, wherein said cell is a human cell.
- 15 43. The method of claim 41, wherein said administration is in the presence of a delivery reagent.
44. The method of claim 43, wherein said delivery reagent is a lipid.
45. The method of claim 44, wherein said lipid is a cationic lipid or a phospholipid.
46. The method of claim 43, wherein said delivery reagent is a liposome.
- 20 47. A nucleic acid molecule that specifically binds the hepatitis B virus (HBV) reverse transcriptase primer, wherein said nucleic acid molecule comprises the sequence (UUCA)_n, wherein n is an integer from 1 to 10.

48. A nucleic acid molecule that specifically binds the hepatitis B virus (HBV) reverse transcriptase primer, wherein said nucleic acid molecule is a sequence comprising any of Seq. ID Nos: 11216-11262, 11264, 11266, 11268, 11270, 11272, 11274, 11276, 11278, 11280, 11282, 11284, 11286, 11288, 11290 and 11292.
- 5 49. A nucleic acid molecule that specifically binds to the Enhancer I sequence of HBV DNA.
50. A nucleic acid molecule of claim 49 wherein said nucleic acid molecule comprises any of SEQ ID Nos: 11327, 11330, 11332, 11334, 11335, 11338, 11340 and 11342.
51. A method of administering to a cell a nucleic acid molecule of any of claims 47-50 comprising contacting said cell with the nucleic acid decoy molecule under conditions
10 suitable for said administration.
52. The method of claim 51, further comprising administering one or more other therapeutic compounds.
53. The method of claim 52, wherein said other therapeutic compound is type I interferon.
54. The method of claim 52, wherein said other therapeutic compound is 3TC® (Lamivudine).
- 15 55. The method of claim 52, wherein said other therapeutic compound and the nucleic acid molecule are administered simultaneously.
56. The method of claim 52, wherein said other therapeutic compound and the nucleic acid molecule are administered separately.
57. The method of claim 53, wherein said type I interferon is selected from the group consisting
20 of interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, and polyethylene glycol consensus interferon.
58. The nucleic acid molecule of any of claims 47-50, wherein said nucleic acid molecule comprises a nucleic acid backbone modification.

59. The nucleic acid molecule of any of claims 47-50, wherein said nucleic acid molecule comprises a nucleic acid sugar modification.
60. The nucleic acid molecule of any of claims 47-50, wherein said nucleic acid decoy molecule comprises a nucleic acid base modification.
- 5 61. The method of claim 51 or claim 52, wherein said cell is a mammalian cell.
62. The method of claim 61, wherein said cell is a human cell.
63. The method of claim 61, wherein said administration is in the presence of a delivery reagent.
64. The method of claim 63, wherein said delivery reagent is a lipid.
65. The method of claim 64, wherein said lipid is a cationic lipid or a phospholipid.
- 10 66. The method of claim 63 wherein said delivery reagent is a liposome.
67. The nucleic acid molecule of claim 47, wherein said nucleic acid molecule is a decoy nucleic acid molecule.
68. The nucleic acid molecule of claim 47, wherein said nucleic acid molecule is an aptamer nucleic acid molecule.
- 15 69. The nucleic acid molecule of claim 49, wherein said Enhancer I sequence comprises a Hepatocyte Nuclear Factor 3 and/or Hepatocyte Nuclear Factor 4 binding sequence.
70. A mouse implanted with HepG2.2.15 cells, wherein said mouse sustains the propagation of HEPG2.2.15 cells and HBV production.
- 20 71. The mouse of claim 70, wherein said mouse has been infected with HBV for at least one week.
72. The mouse of claim 70, wherein said mouse has been infected with HCV for at least four weeks.
73. The mouse of claim 70, wherein said mouse has been infected with HBV for at least eight weeks.

74. The mouse of claim 70, wherein said mouse is an immuno compromised mouse.
75. The mouse of claim 74, wherein said mouse is a nu/nu mouse.
76. The mouse of claim 74, wherein said mouse is a scid/scid mouse.
- 5 77. A method of producing a mouse according to claim 70, comprising injecting HepG2.2.15 cells into said mouse under conditions suitable for the propagation of the HepG2.2.15 cells in said mouse.
78. The method of claim 77, wherein said mouse is a nu/nu mouse.
79. The method of claim 77, wherein said mouse is a scid/scid mouse.
80. The method of claim 77, wherein said injection is subcutaneous injection.
- 10 81. The method of claim 77, wherein said HepG2.2.15 cells are suspended in Dulbecco's PBS solution including calcium and magnesium.
82. A method of screening a therapeutic compound for activity against HBV comprising administering said therapeutic compound to a mouse of claim 70 and monitoring said mouse for the effects of said therapeutic compound on levels of HBV DNA.
- 15 83. The method of claim 70, wherein said therapeutic compound is a nucleic acid molecule, administered alone or in combination with another therapeutic compound or treatment.
84. The method of claim 83, wherein said nucleic acid molecule is an enzymatic nucleic acid molecule.
85. The method of claim 83, wherein said nucleic acid molecule is an antisense nucleic acid
20 molecule.
86. The method of claim 83, wherein said other treatment is antiviral therapy.
87. The method of claim 86, wherein said antiviral therapy is treatment with 3TC® (Lamivudine).
88. The method of claim 86, wherein said antiviral therapy is treatment with interferon.
- 25 89. The method of claim 88, wherein said interferon is selected from the group consisting of consensus interferon, type I interferon, interferon alpha, interferon beta, consensus

interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b and polyethylene glycol consensus interferon.

- 5 90. An immunocompromised non-human mammal implanted with HepG2.2.15 cells, wherein said non-human mammal is susceptible to HBV infection and capable of sustaining HBV DNA expression.
91. The mammal of claim 90, wherein said non-human mammal has been infected with HBV for at least one week.
92. The mammal of claim 90, wherein said non-human mammal has been infected with HCV for at least four weeks.
- 10 93. The mammal of claim 90, wherein said non-human mammal has been infected with HBV for at least eight weeks.
94. The mammal of claim 90, wherein said non-human mammal is a nu/nu mammal.
95. The mammal of claim 90, wherein said non-human mammal is a scid/scid mammal.
- 15 96. A method of producing a non-human mammal according to claim 90, comprising injecting HepG2.2.15 cells into said non-human mammal under conditions suitable for the propagation of the HepG2.2.15 cells in said non-human.
97. The method of claim 96, wherein said non-human mammal is a nu/nu mammal.
98. The method of claim 96, wherein said non-human mammal is a scid mammal.
99. The method of claim 96, wherein said injection is subcutaneous injection.
- 20 100. The method of claim 96, wherein said HepG2.2.15 cells are suspended in Delbecco's PBS solution including calcium and magnesium.
101. A method of screening a therapeutic compound for activity against HBV, comprising administering said therapeutic compound to a non-human mammal of claim 90 and monitoring said mammal for the effects of said therapeutic compound on levels of HBV DNA.
- 25 102. The method of claim 101, wherein said therapeutic compound is a nucleic acid molecule administered alone or in combination with another therapeutic compound or treatment.

103. The method of claim 102, wherein said nucleic acid molecule is an enzymatic nucleic acid molecule.

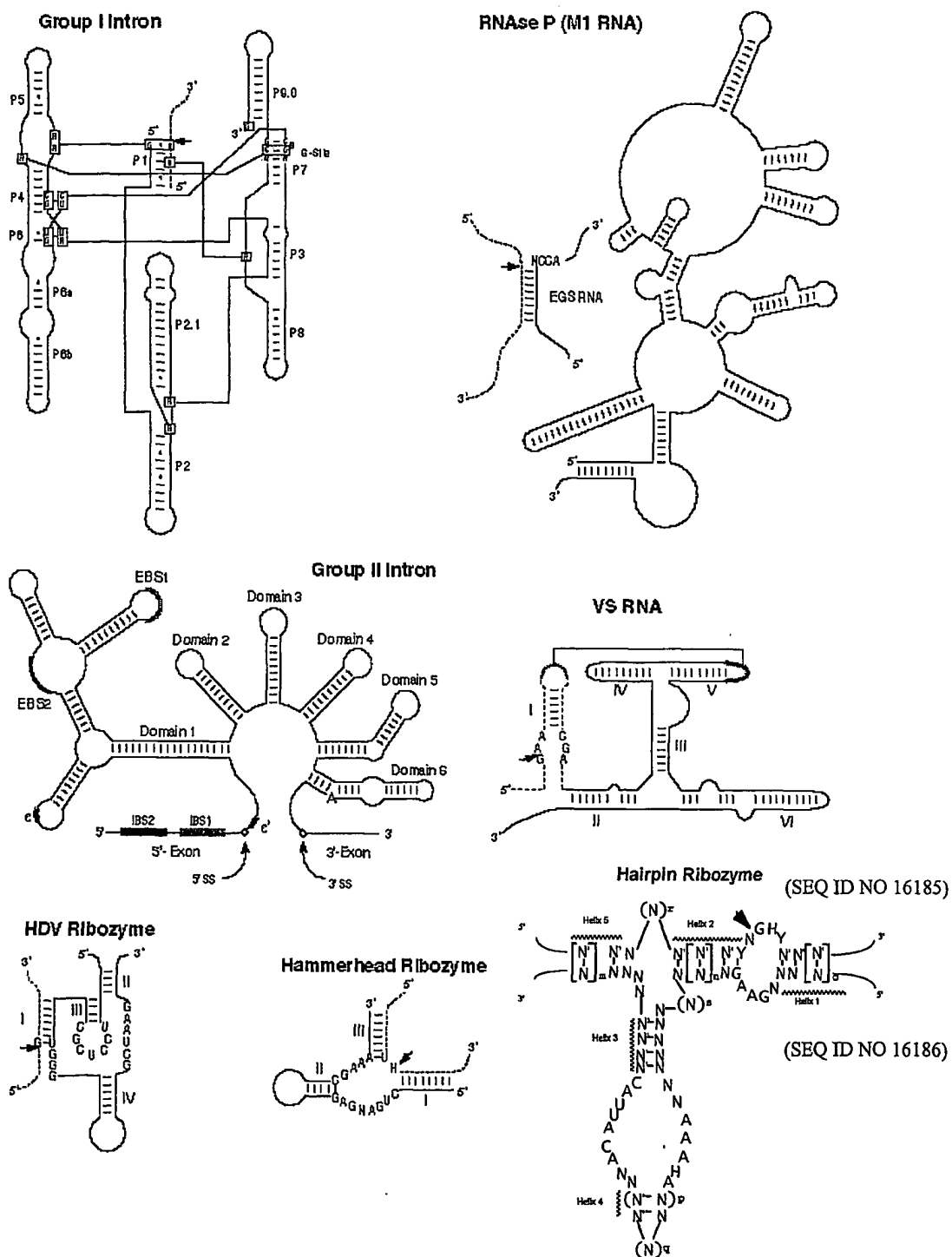
104. The method of claim 102, wherein said nucleic acid molecule is an antisense nucleic acid molecule.

5 105. The method of claim 102, wherein said other treatment is antiviral therapy.

106. The method of claim 105, wherein said antiviral therapy is treatment with 3TC® (Lamivudine).

107. The method of claim 105, wherein said antiviral therapy is treatment with interferon.

10 108. The method of claim 107, wherein said interferon is selected from the group consisting of consensus interferon, type I interferon, interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, and polyethylene glycol consensus interferon.

Figure 1: Ribozyme Motifs

[illegible]

Figure 3: 2'-O-Me substituted Amberzyme Enzymatic Nucleic Acid Motif

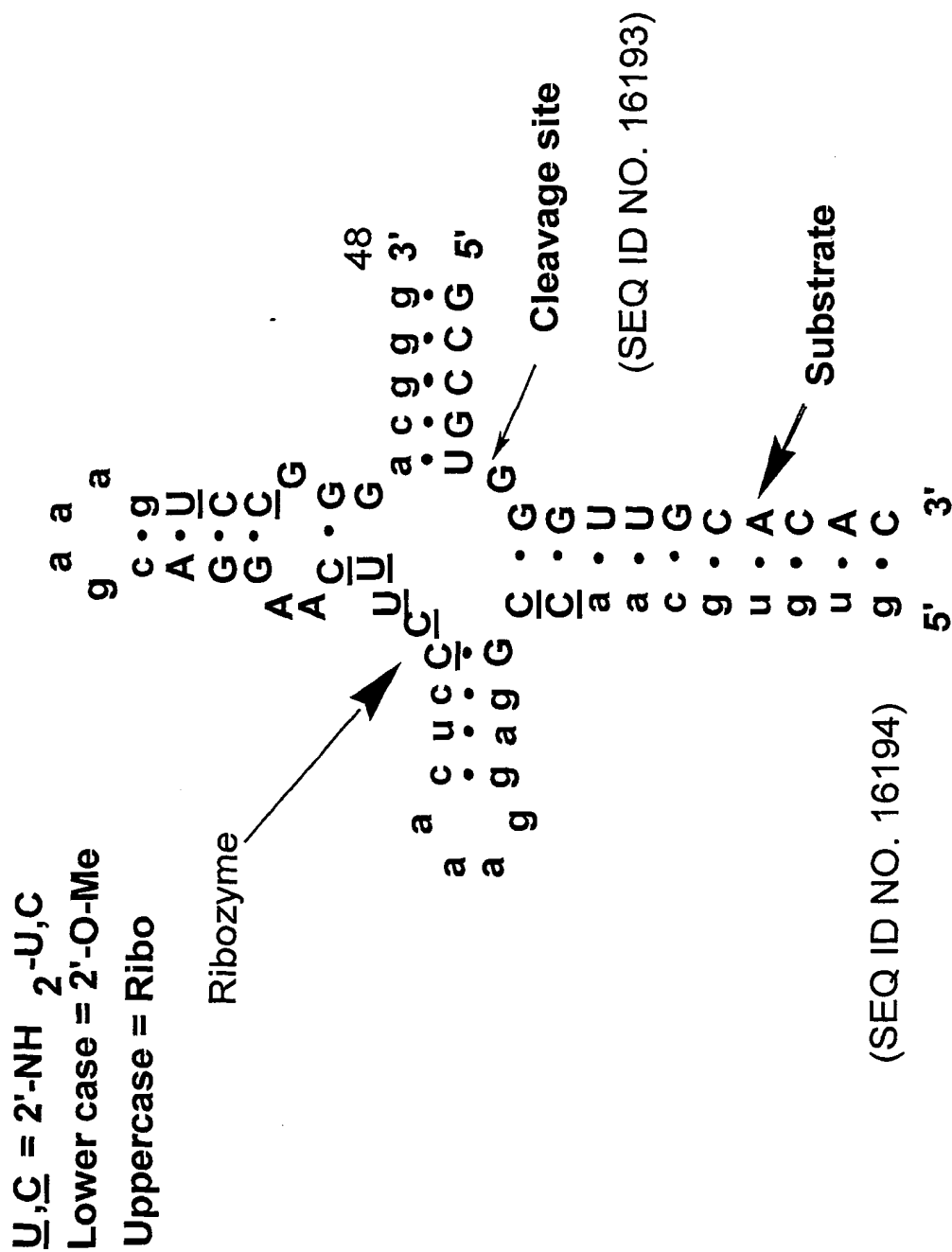
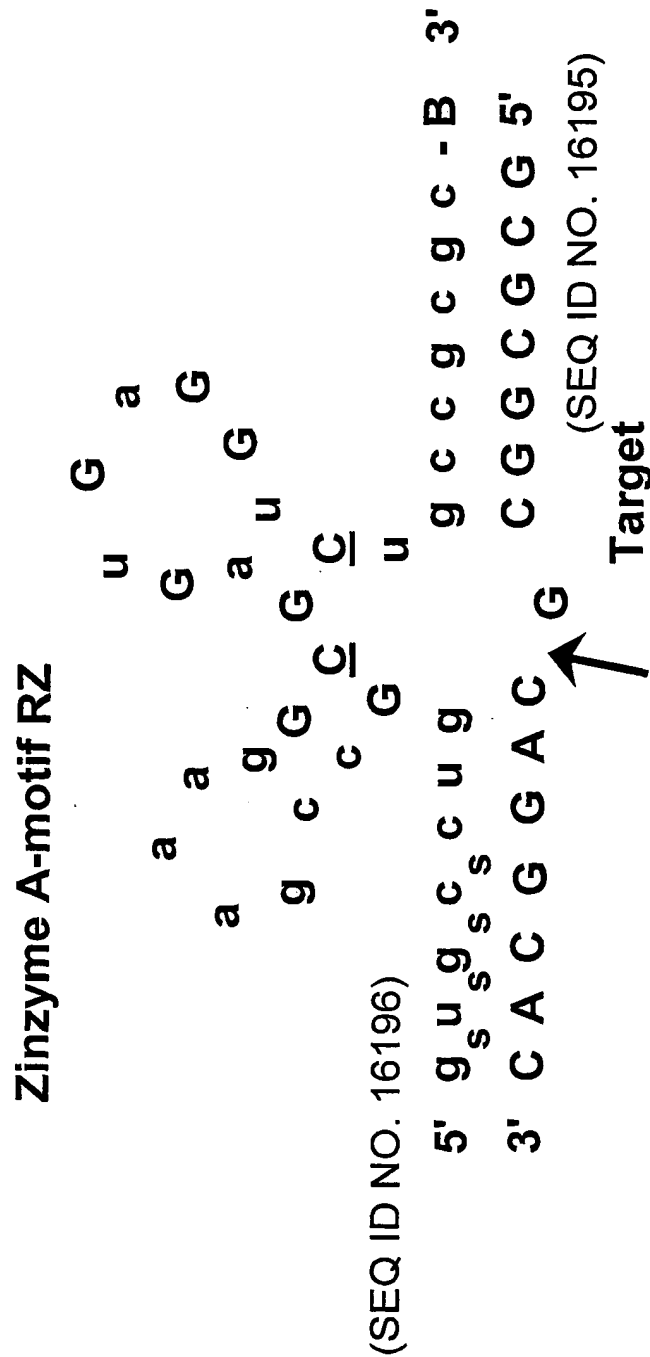


Figure 4: Stabilized Zinzyme Ribozyme Motif



Legend

Uppercase indicates natural ribo residues

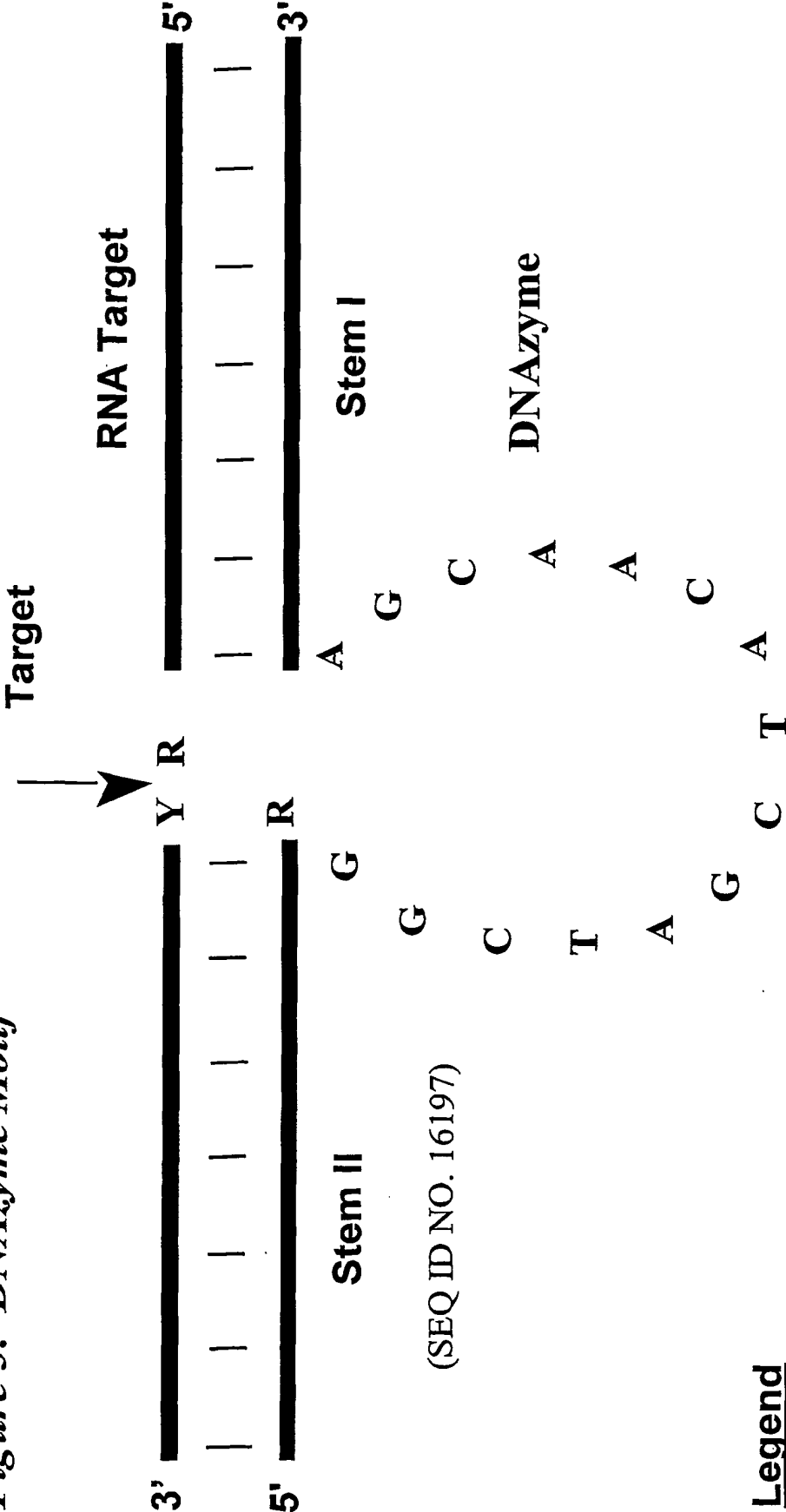
C indicates 2'- d-NH₂-C

Lowercase: 2'-O-Me

Subscript _s indicates phosphothioate linkage

B: 3'- 3' abasic moiety

Figure 5: DNAzyme Motif



(SEQ ID NO. 16197)

Legend
Y = U or C
R = A or G

Figure 6: Change in Serum HBV DNA Levels Following 14 Days of Ribozyme Treatment of HBV Transgenic Mice

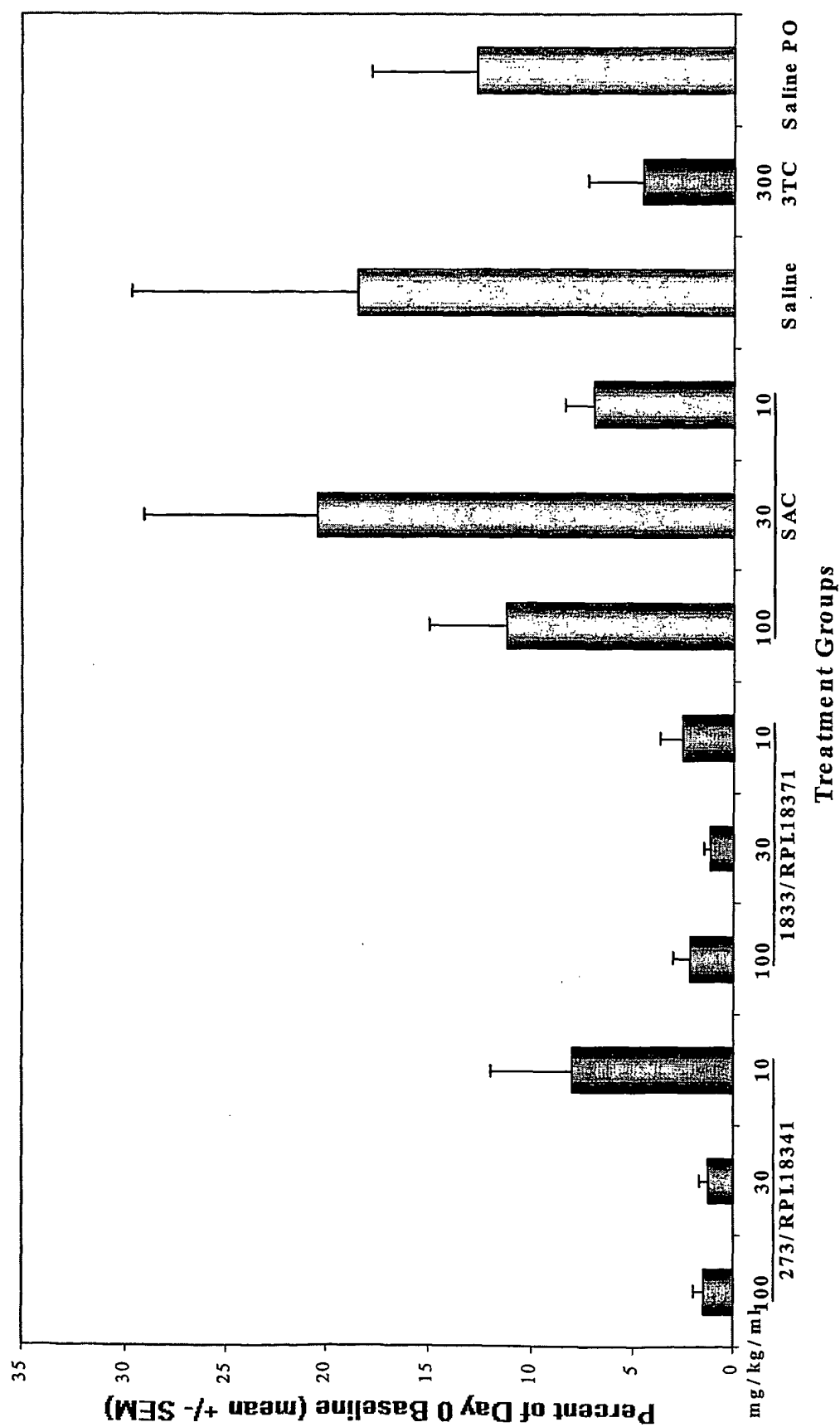


Figure 7: Mean Serum HBV DNA Levels Following 14 Days of Ribozyme Treatment of HBV Transgenic Mice

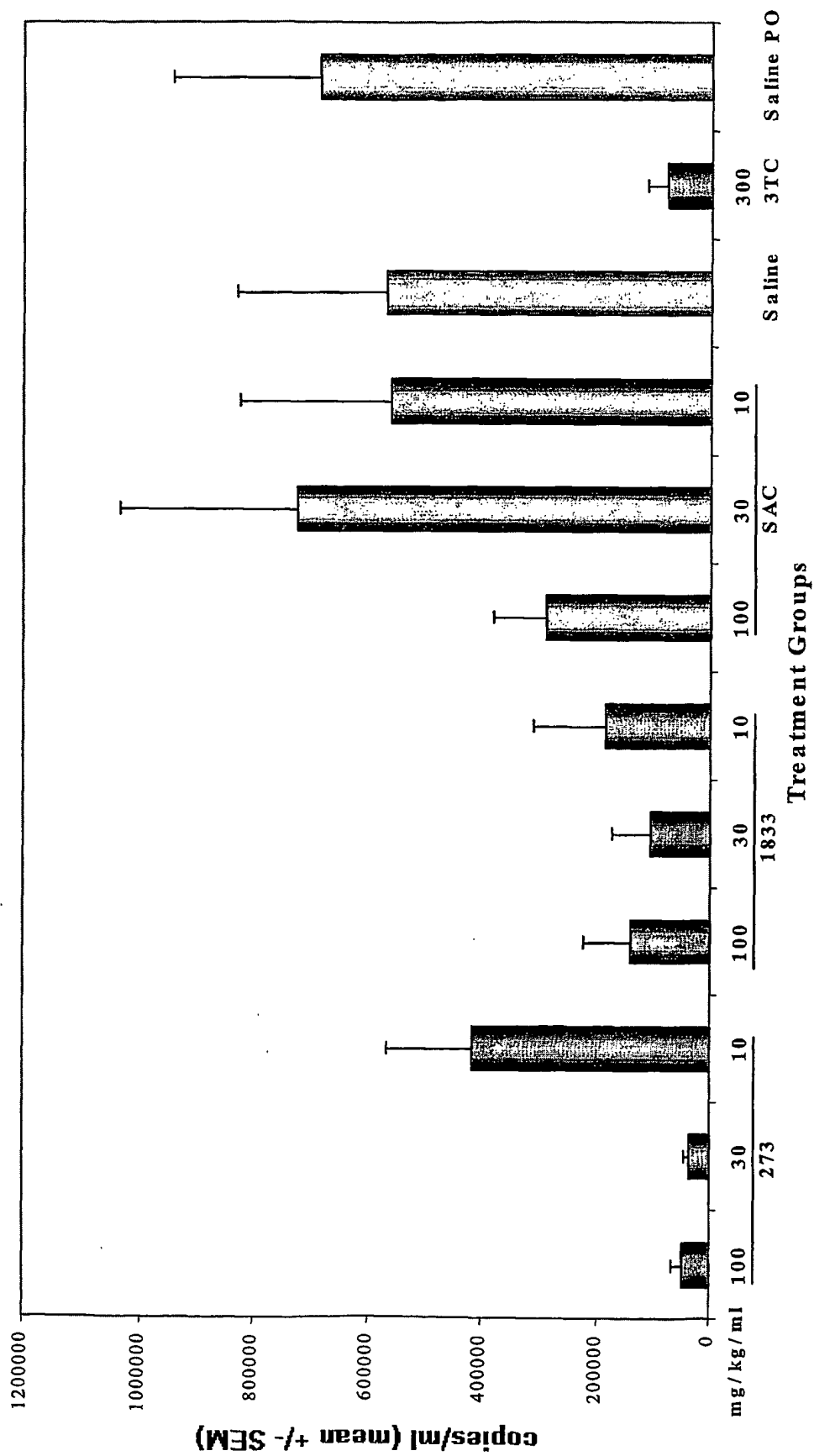


Figure 8: Change in Serum HBV DNA Levels (Log) Following 14 Days of Ribozyme Treatment of HBV Transgenic Mice

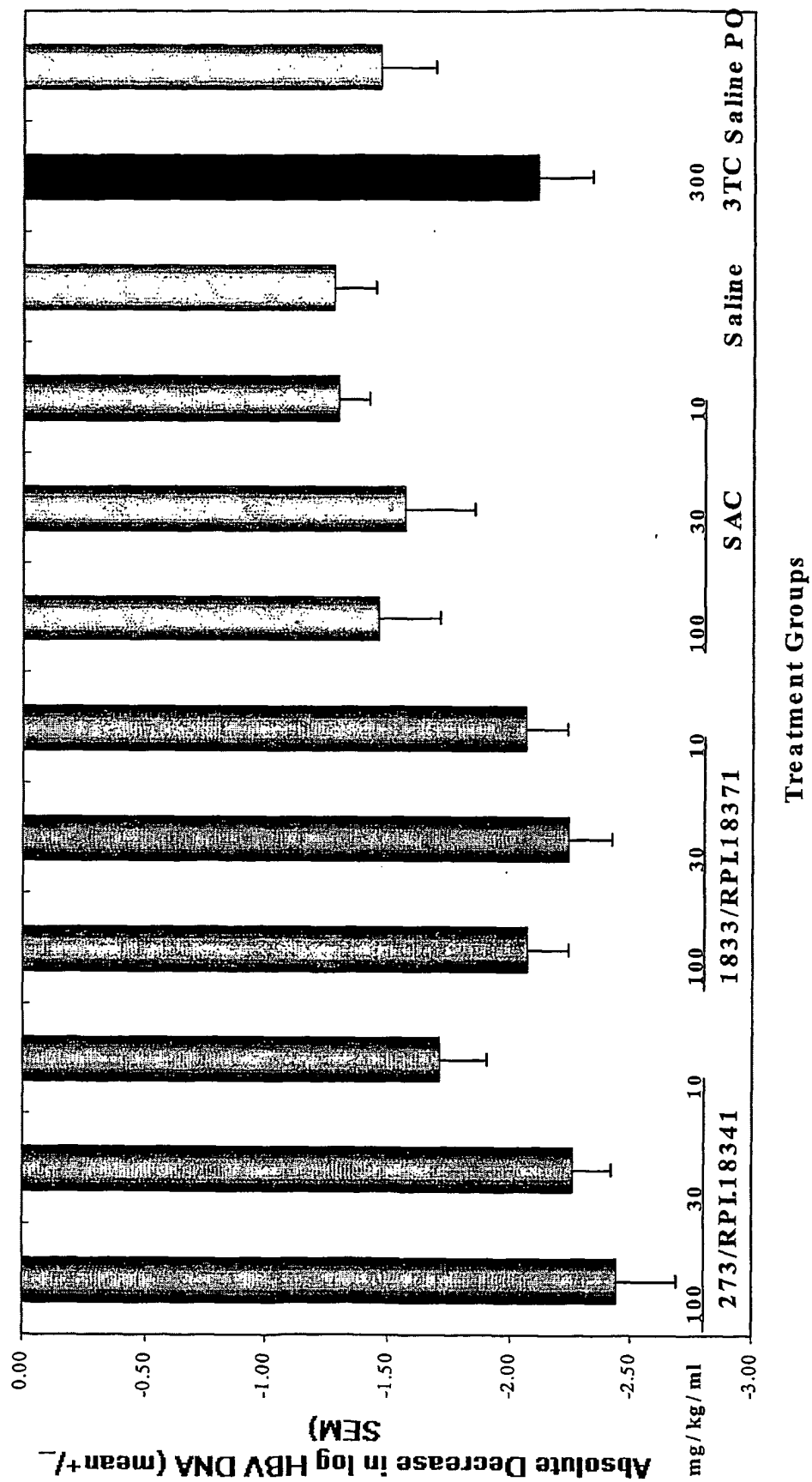


Figure 9: anti-HBV Ribozymes in HepG2.2.15 Cells: HBV DNA

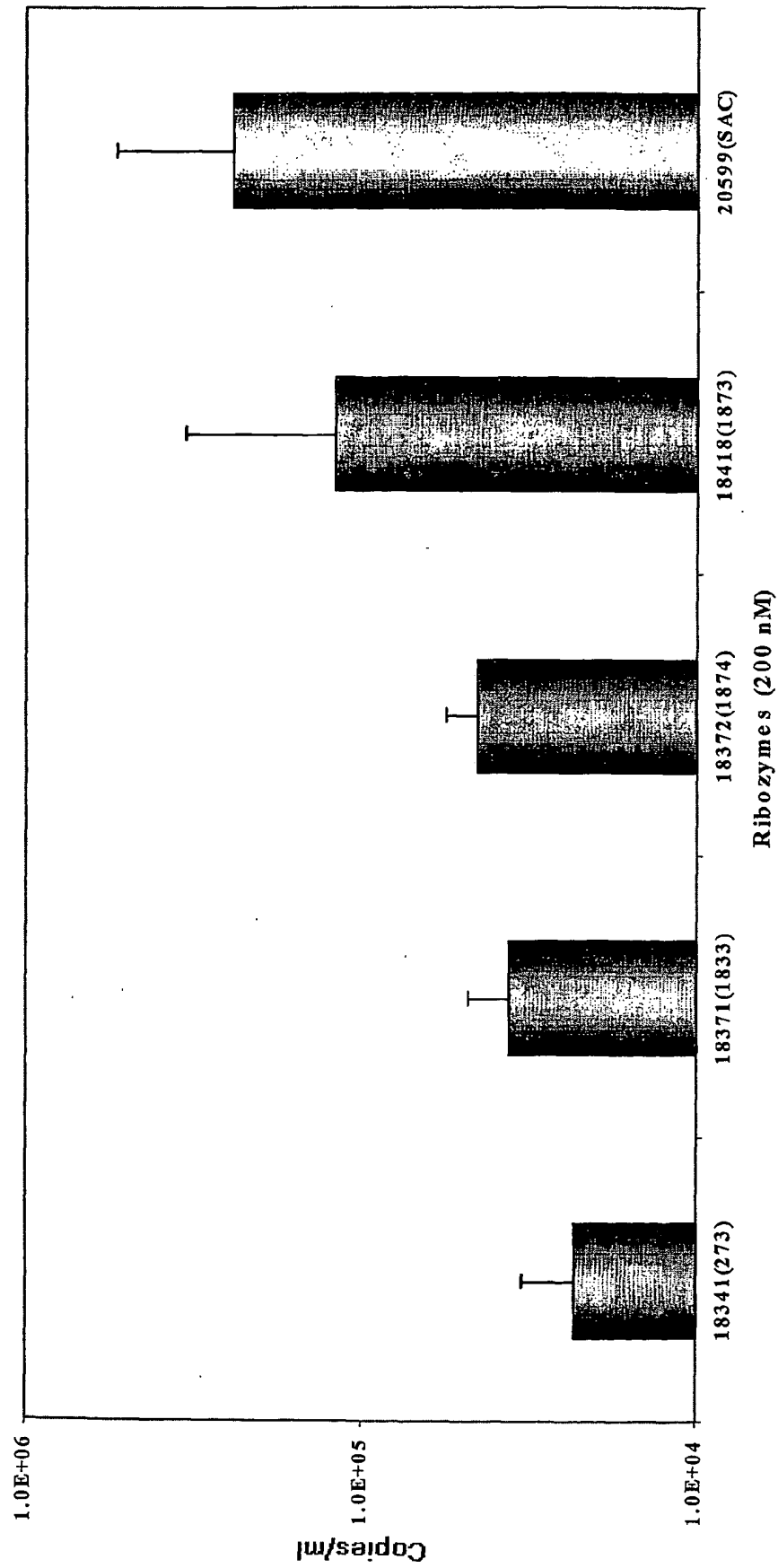


Figure 10: Arm, Loop, and Stem Variants of Anti-HBV Ribozyme Targeting Site 273: HBsAg Levels in Hep G2 Cells

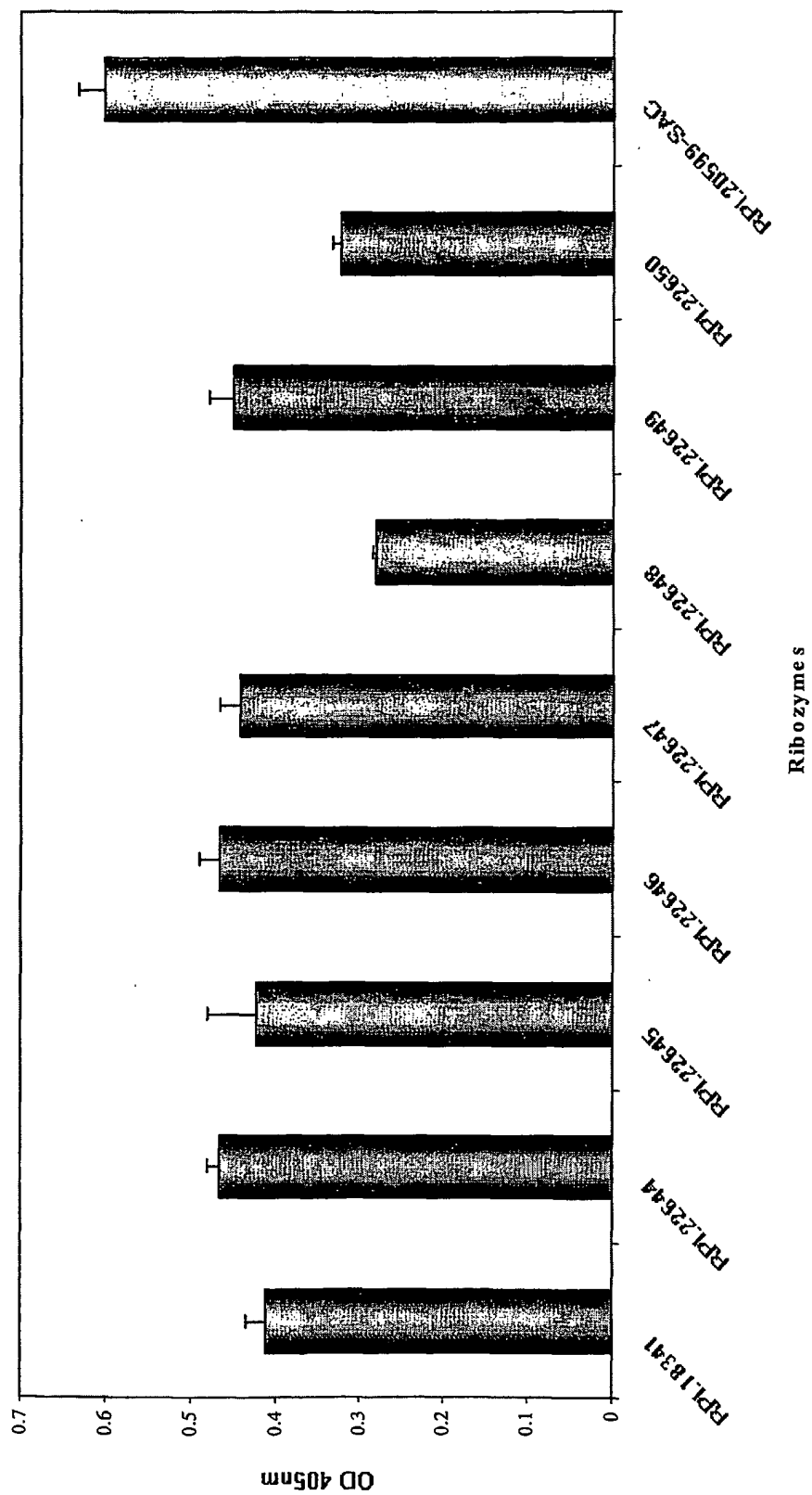


Fig 11: Hep G2 Cells Treated with RPI.18341
and Interferon: HBsAg ELISA

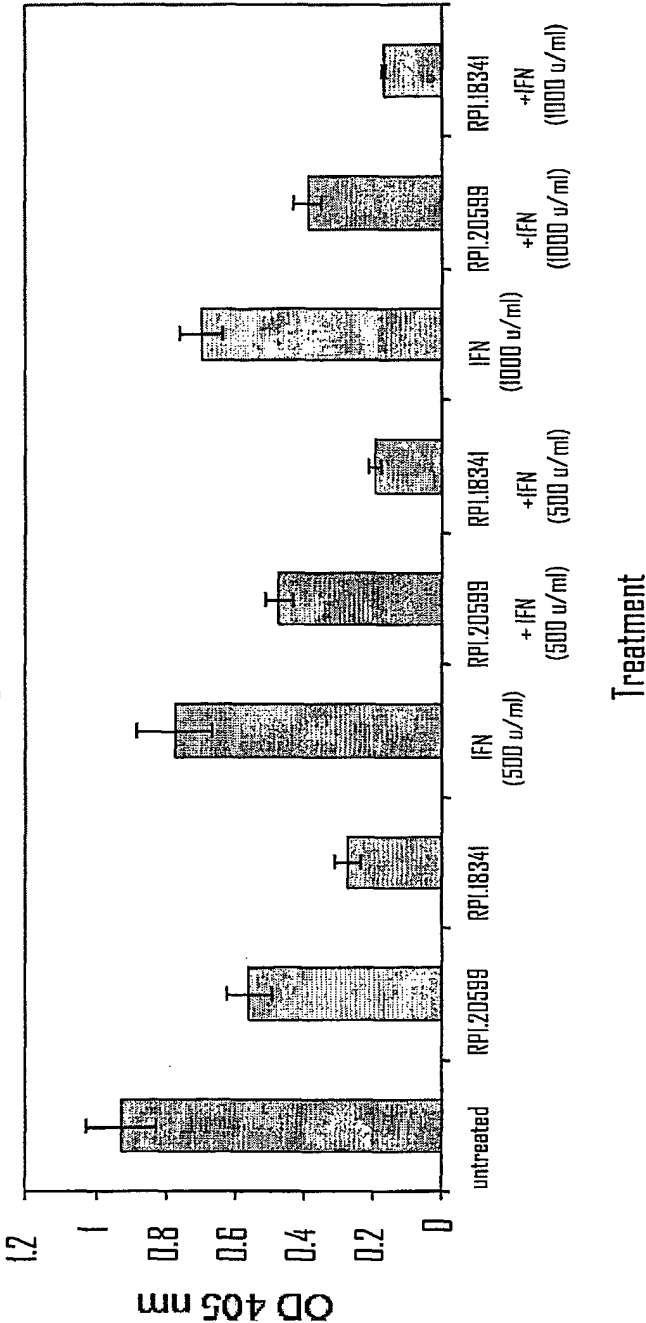


Fig 12: Hep G2 Cells Treated with 100 nM RPI.18341 and Lamivudine (3TC): HBsAg ELISA

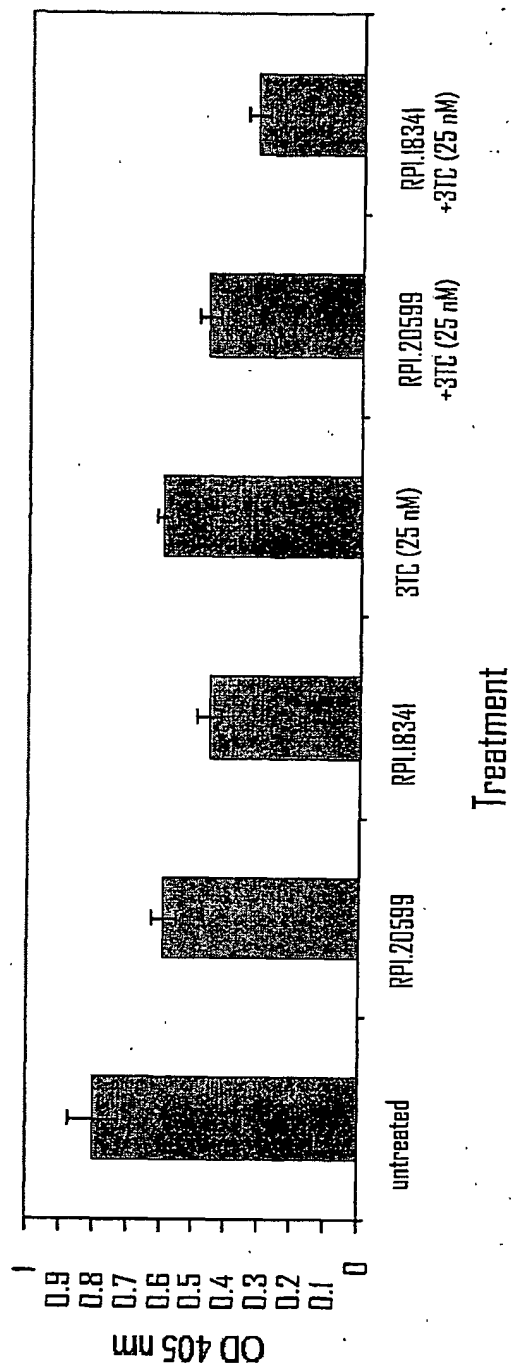


Figure 13: HBV Reverse Transcription

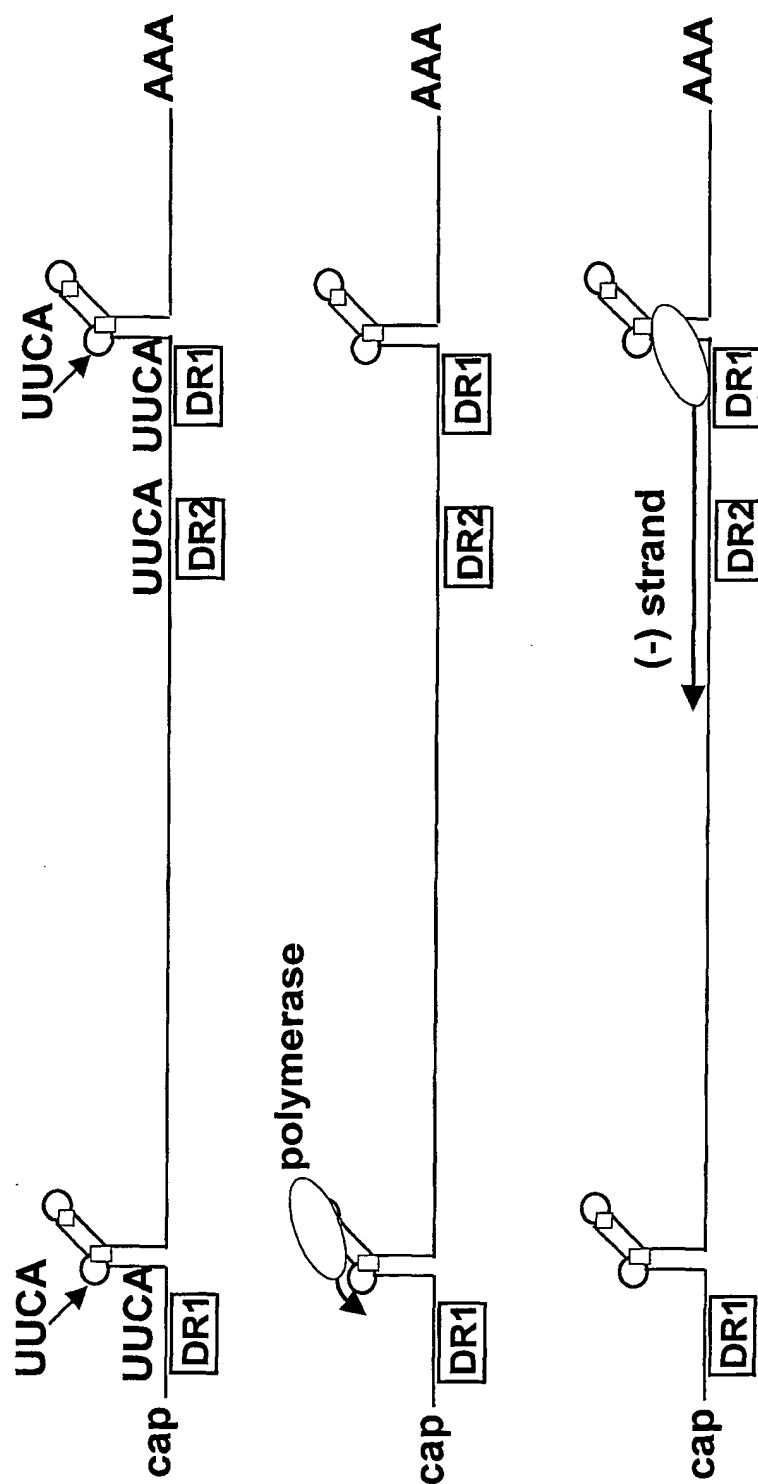


Figure 14: HBV RT Inhibition

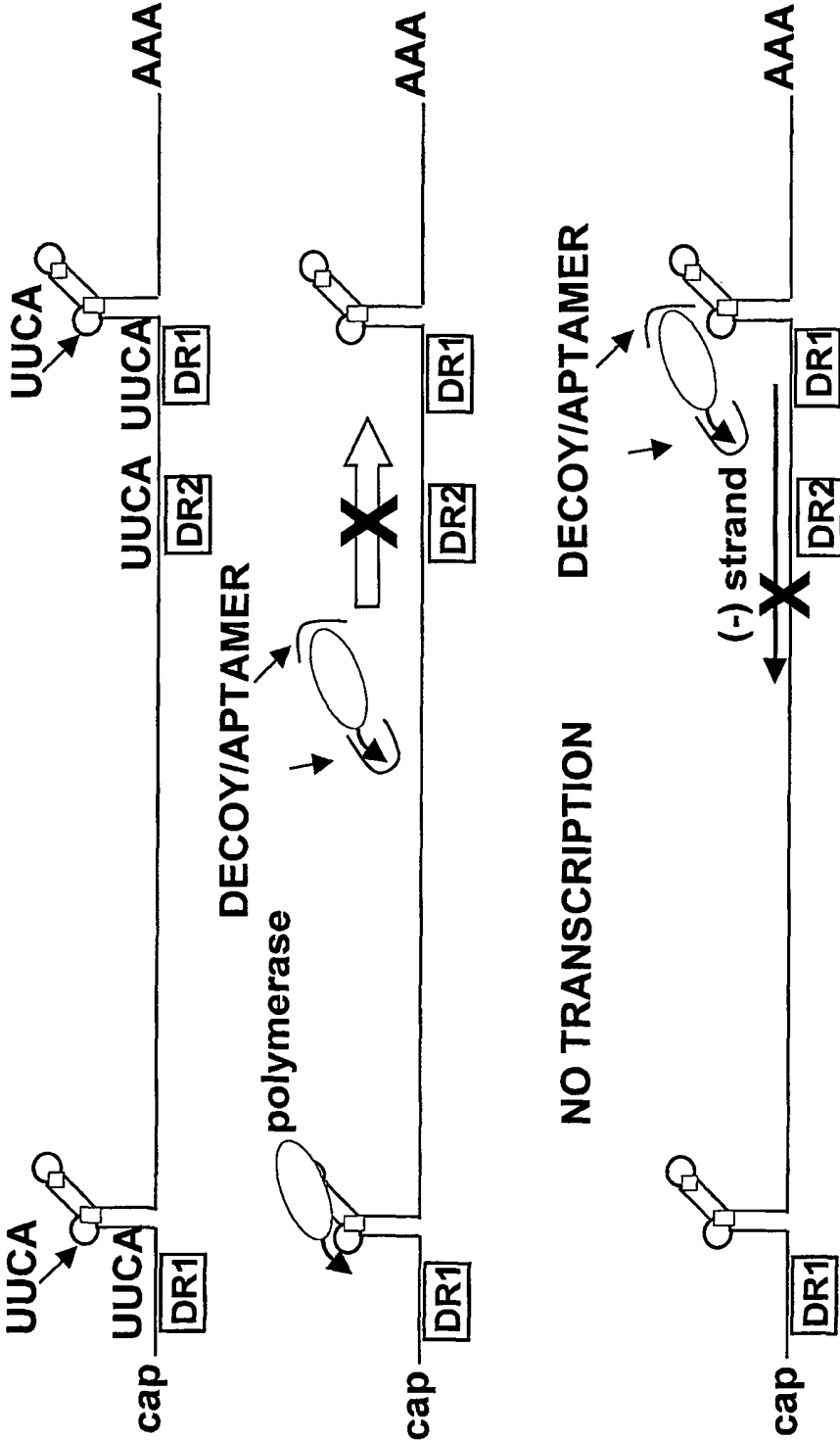


Figure 15: Screening of HBV RT Primer Competitive Inhibitors (2'-O-Allyl): HBsAg

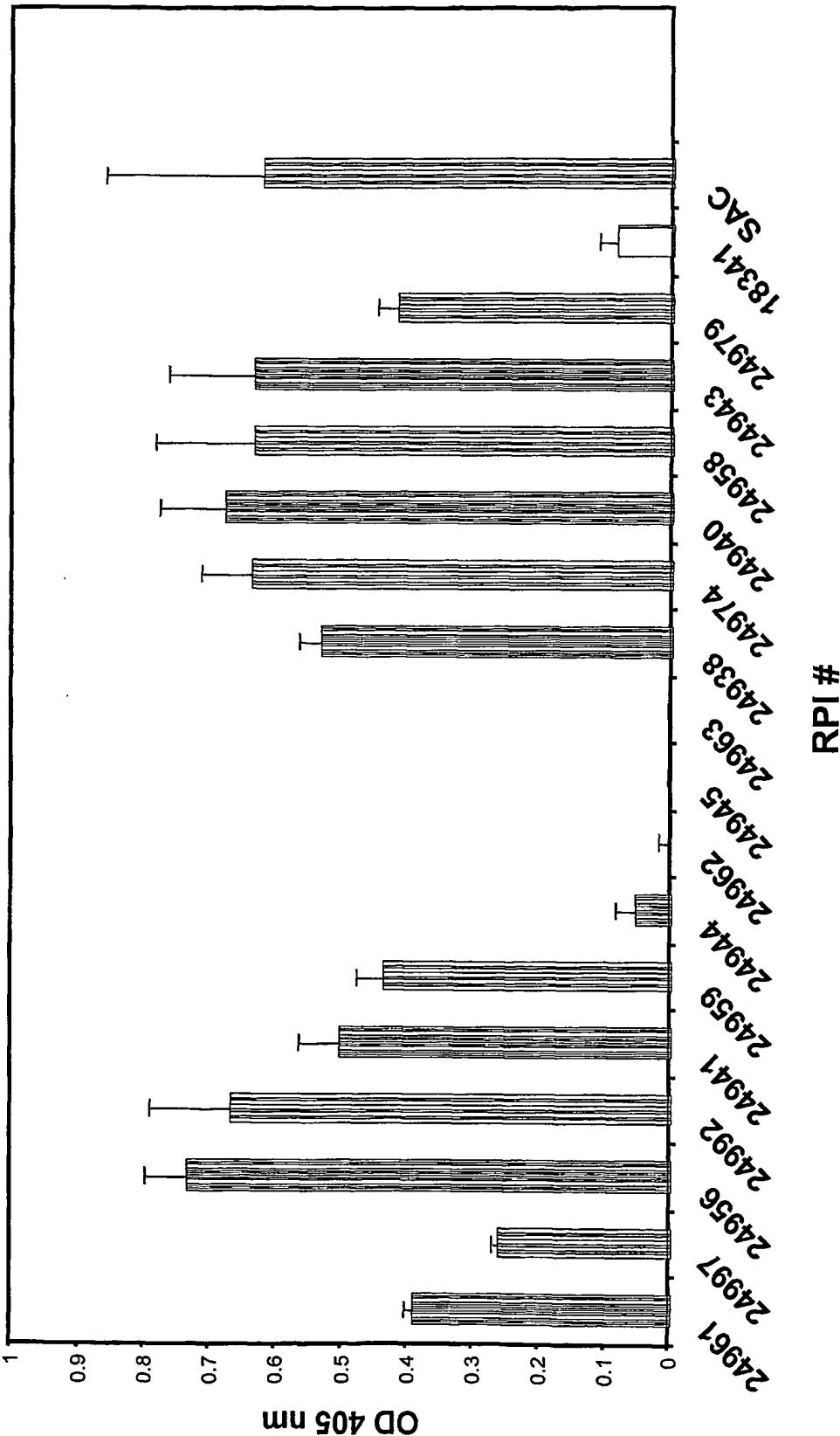
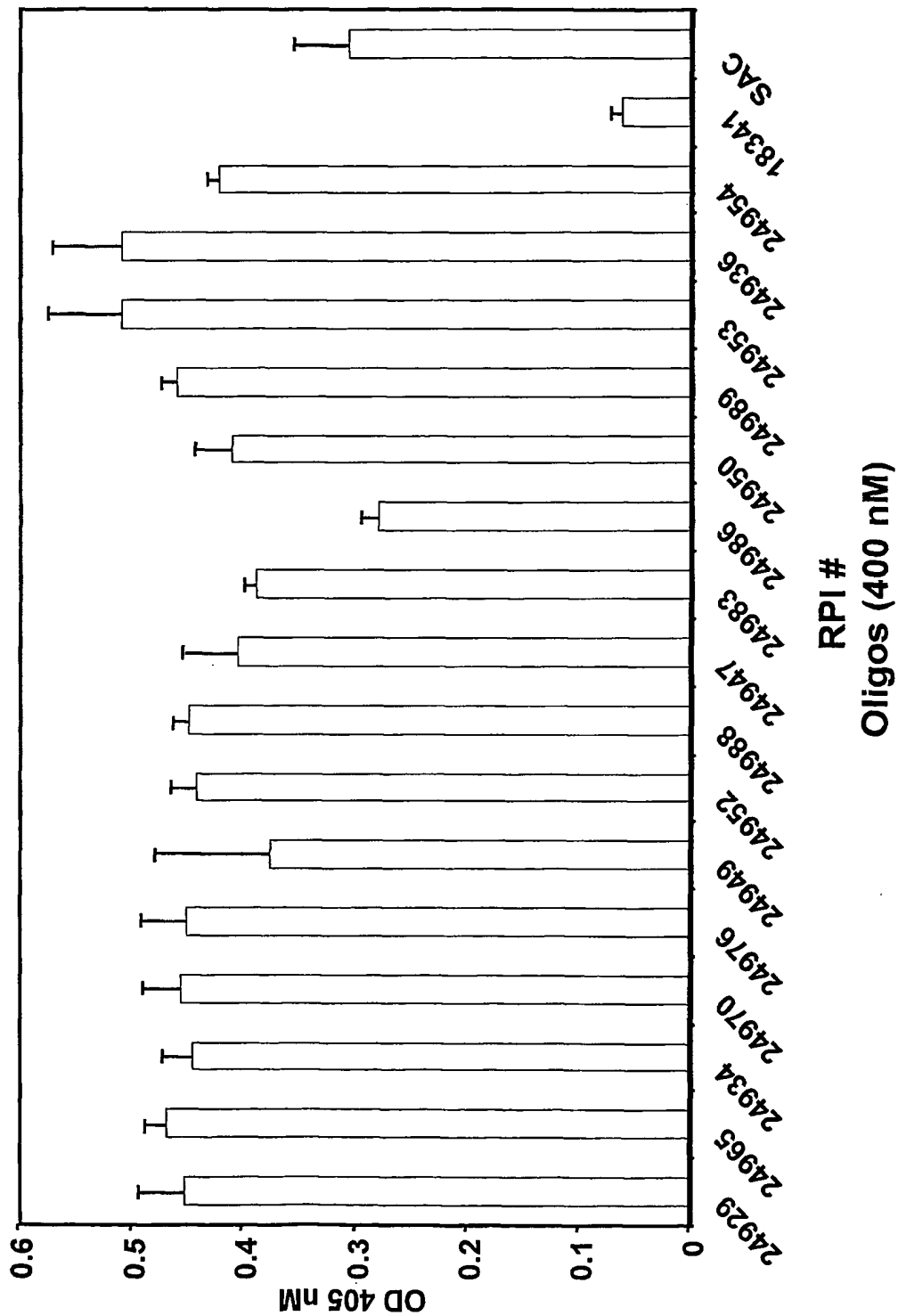


Figure 16: Screening of HBV RT Primer Competitive Inhibitors (2'-O-Methyl): HBsAg



**Figure 17: Dose Response with 2'-O-Methyl
UUCAUUA Oligo: HBsAg**

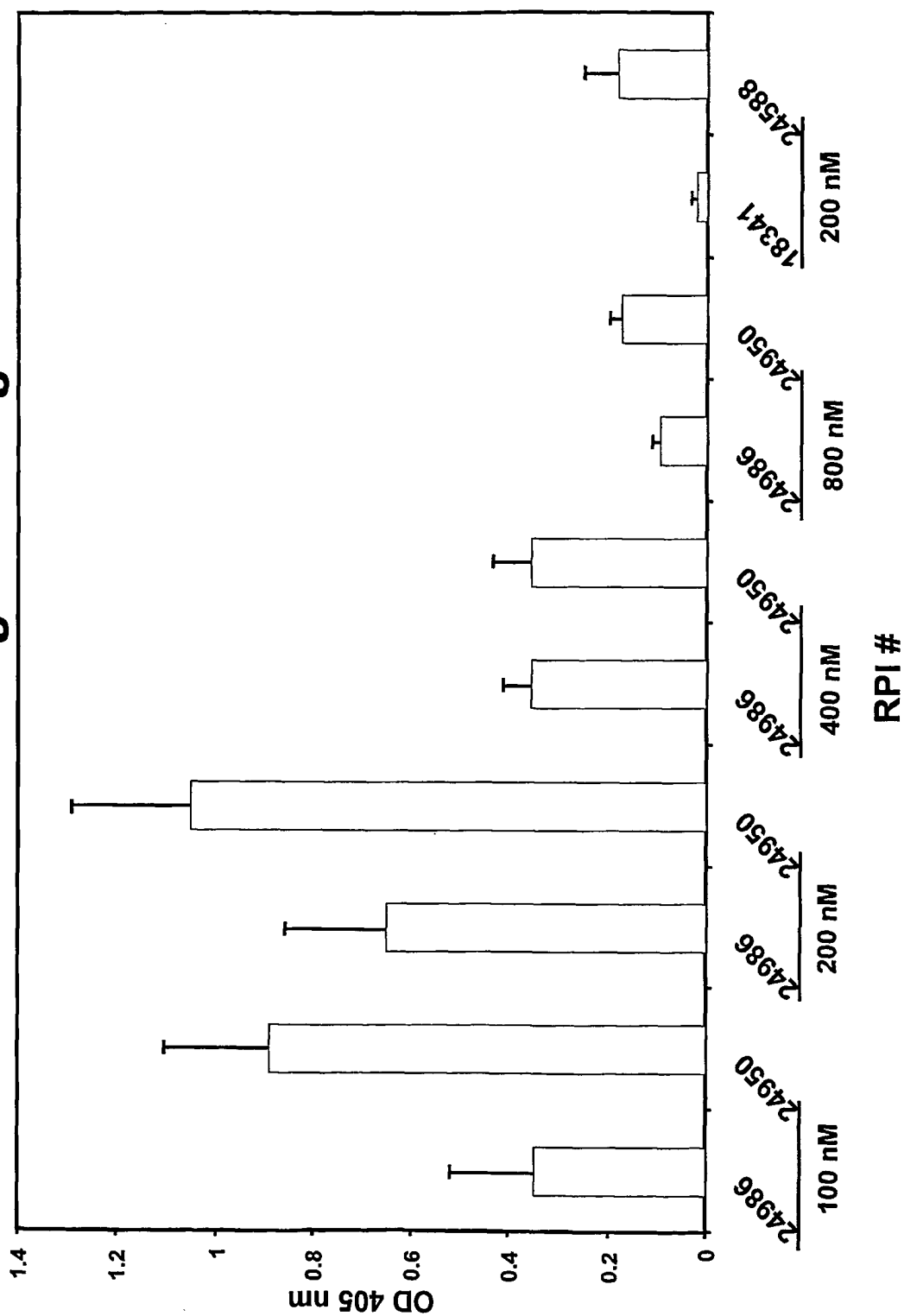


Figure 18: HBV Enhancer I Oligo Screen 200 nM:HBsAg

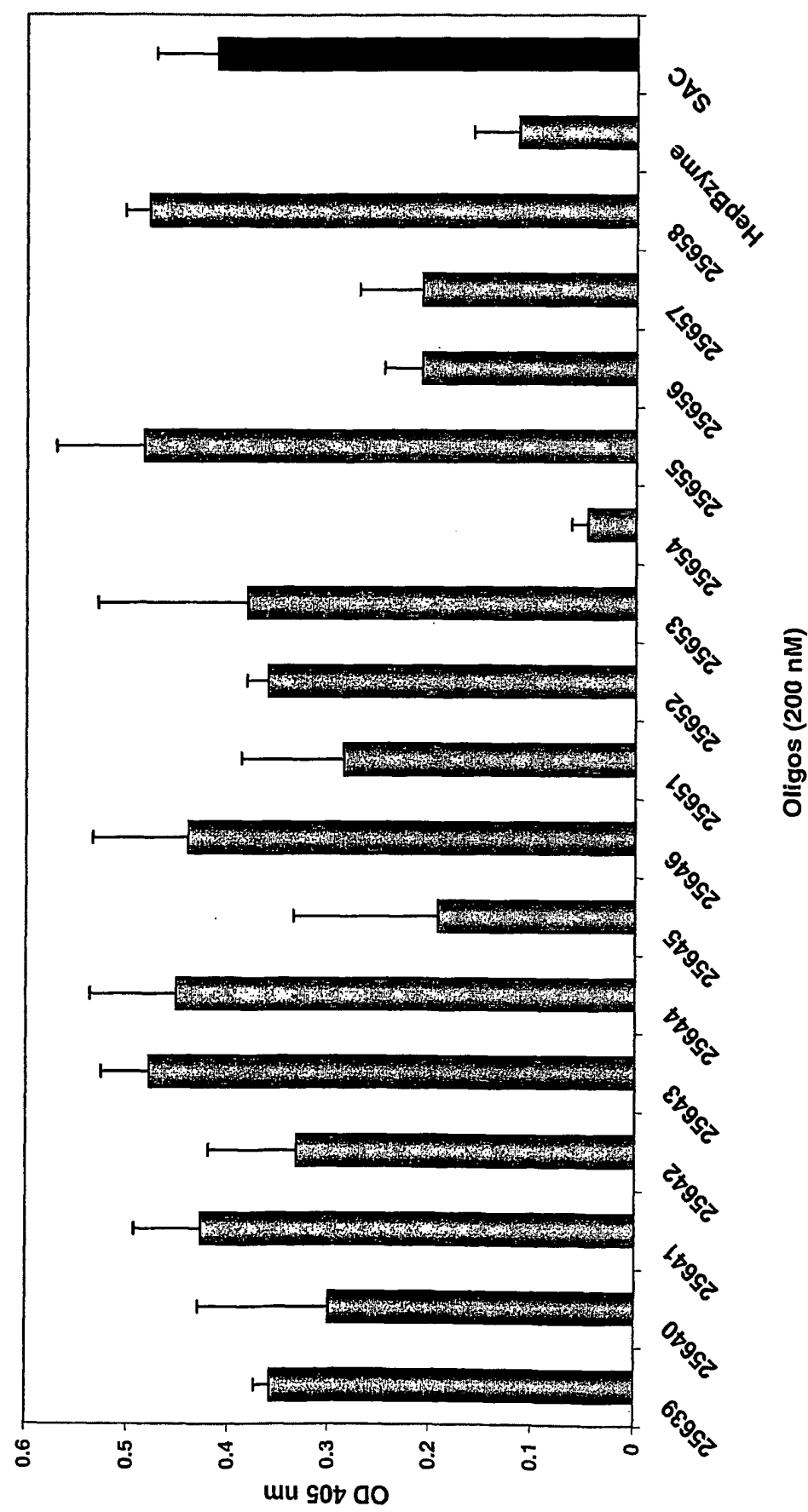


Figure 19: HBV Enhancer I Oligo Screen 400 nM: HBsAg

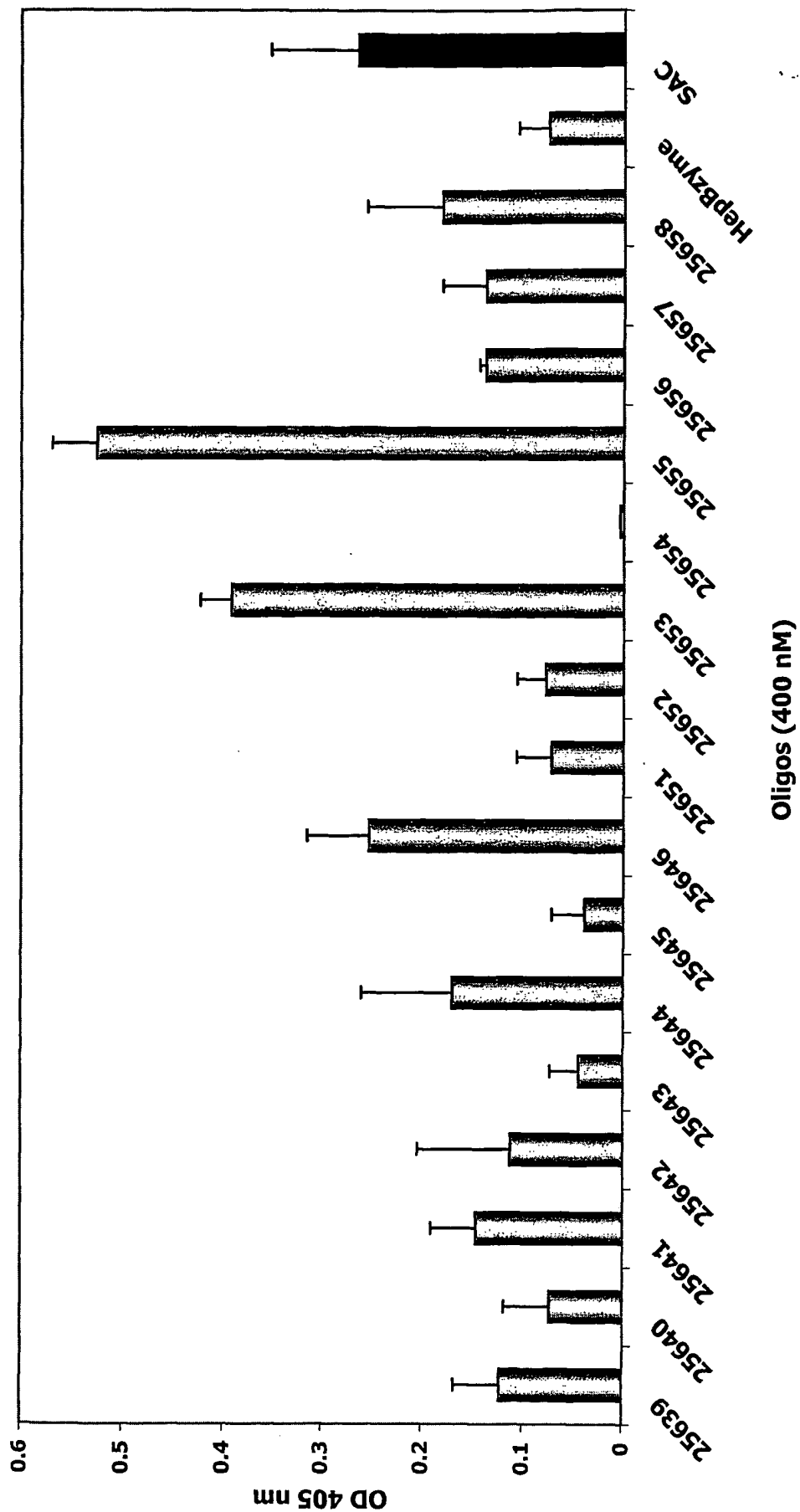
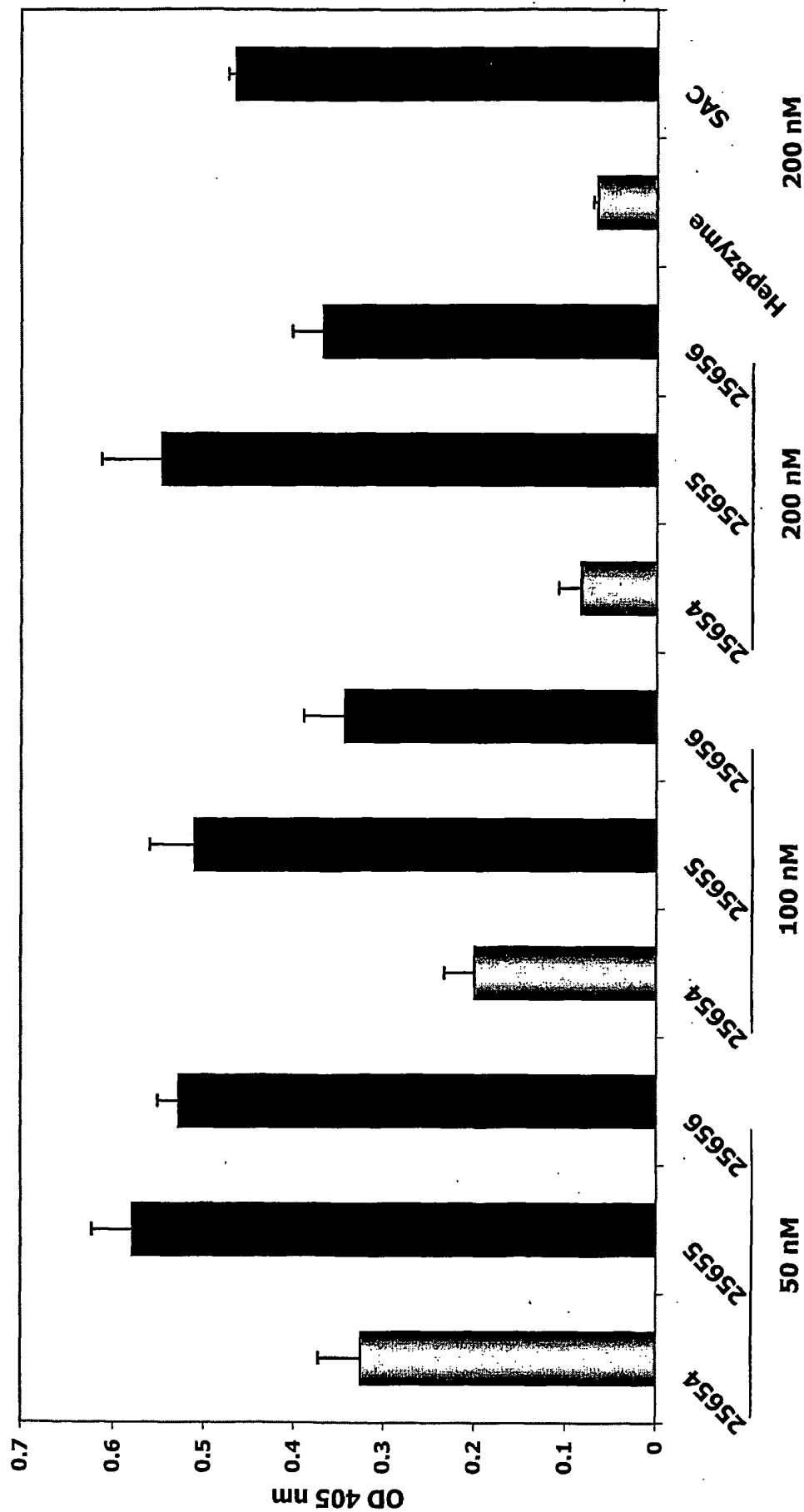
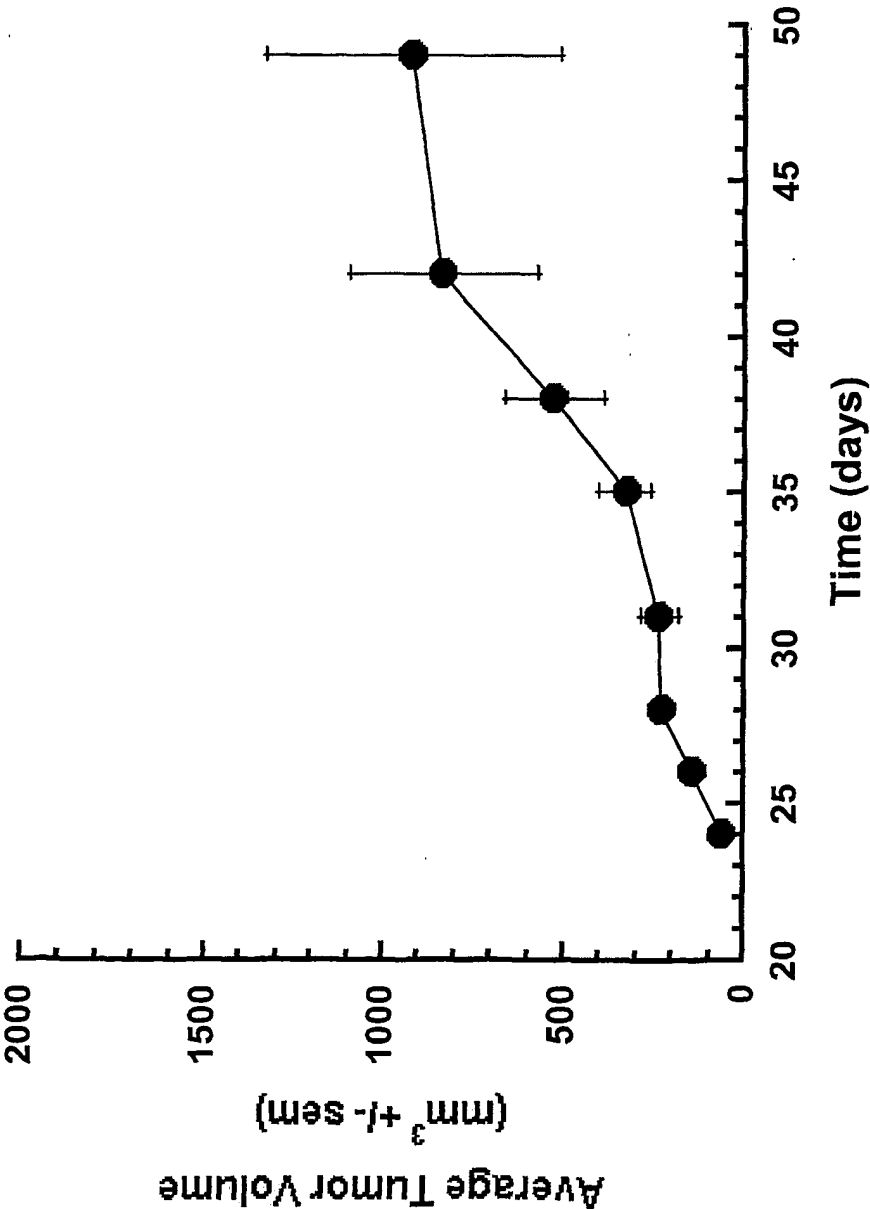


Figure 20: HBV Enhancer 1 Oligos Dose Response HBsAg



**Figure 21: Growth of HepG2.2.15 tumors in
Athymic Nu/Nu female mice**



**Figure 22: Growth of HepG2.2.15 tumors in
Athymic Nu/Nu female mice**

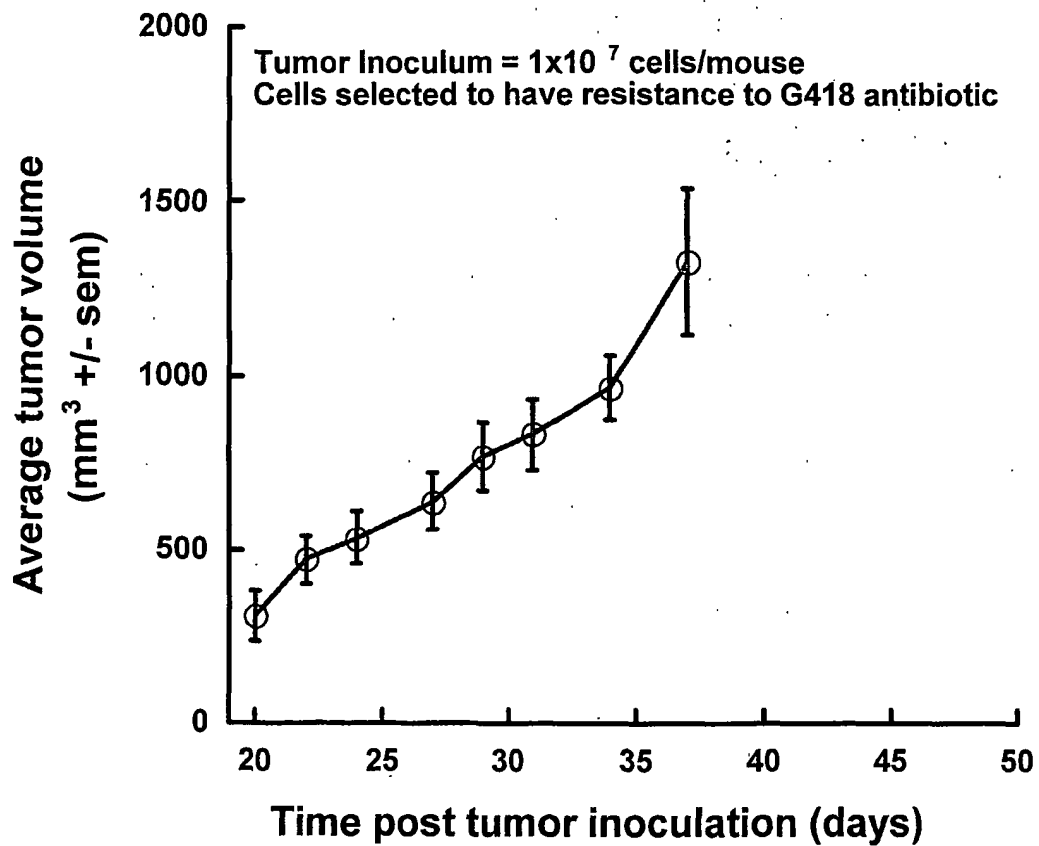


FIGURE 23 *Dual Reporter System for Cytoplasmic HCV Target*

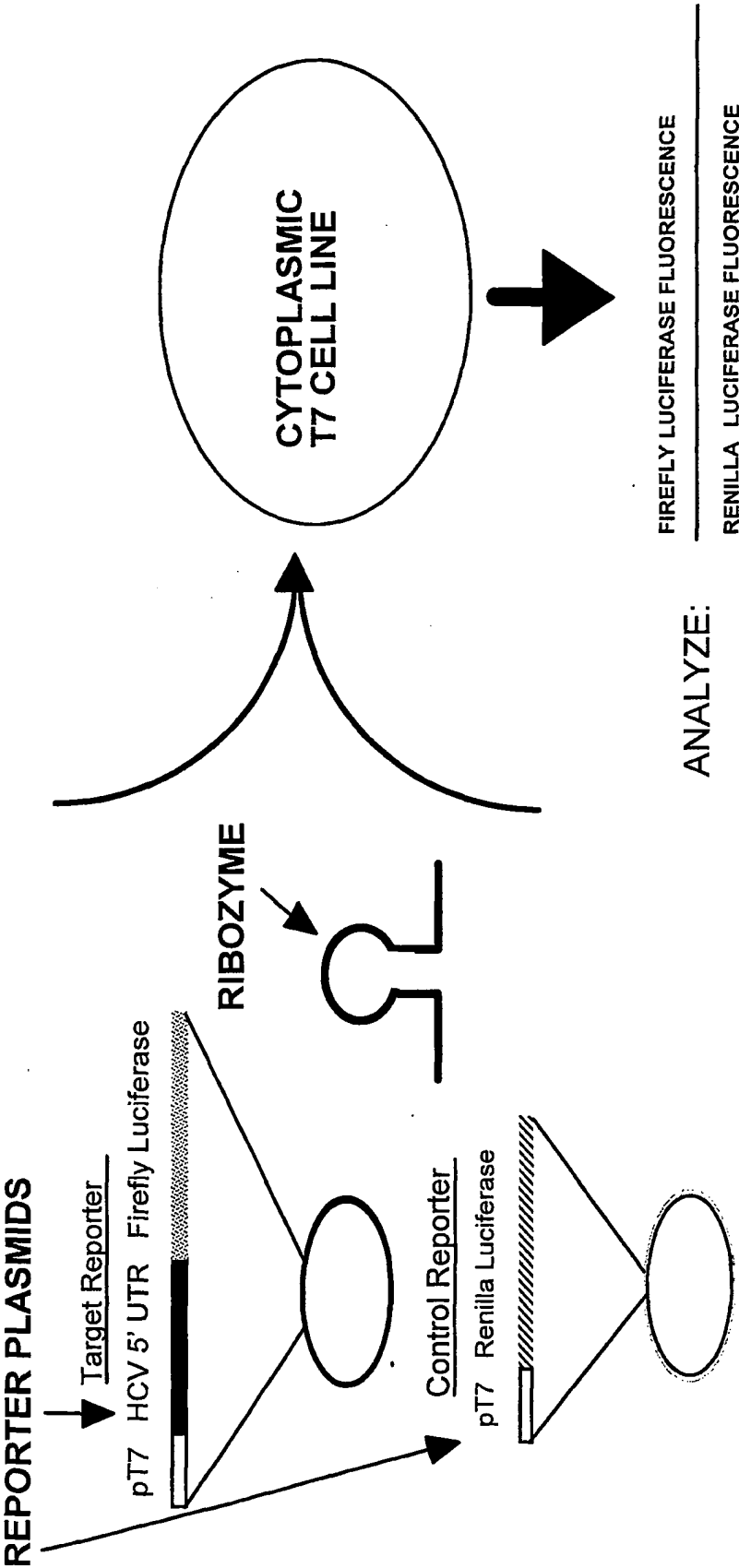
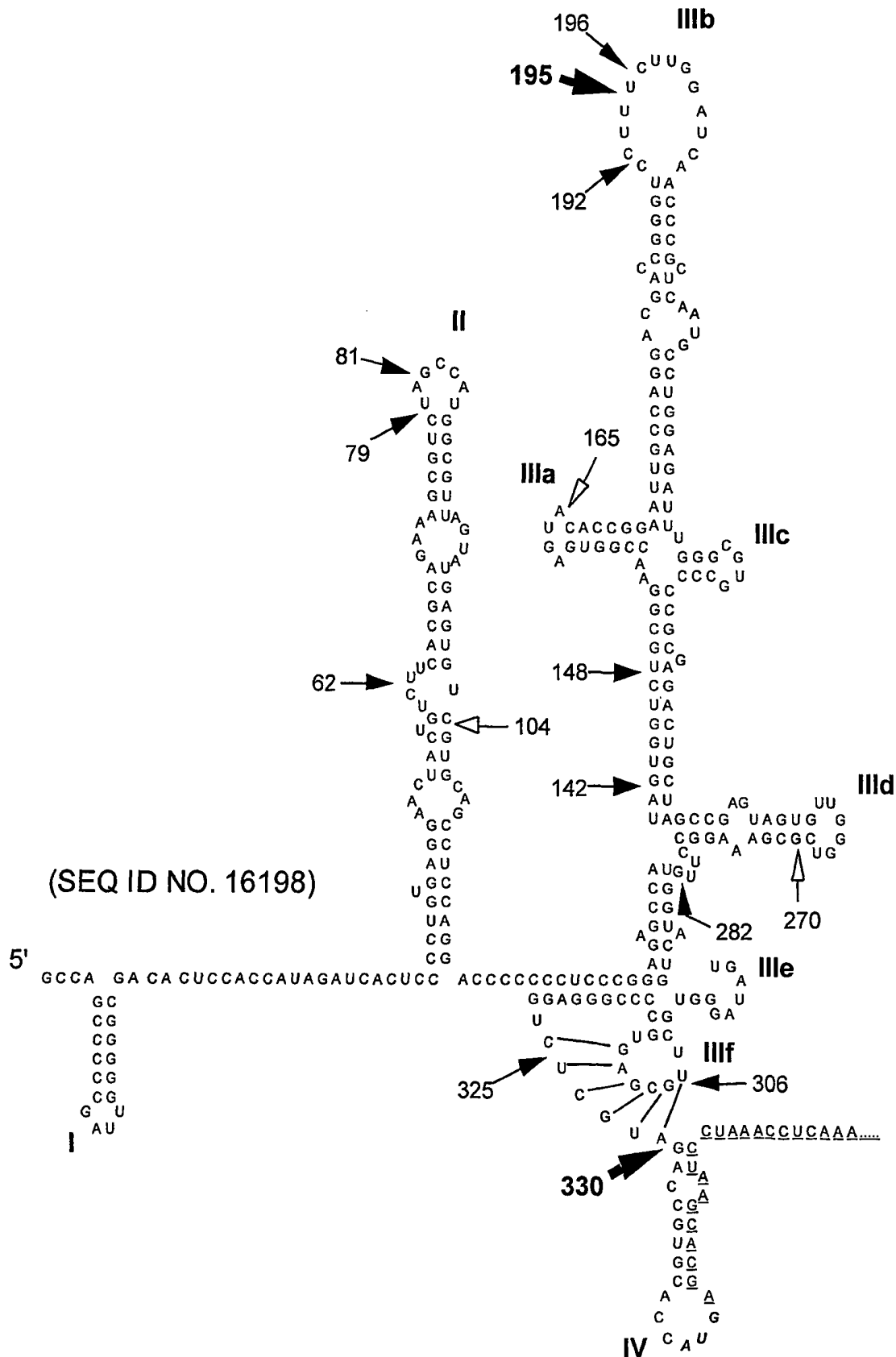


Figure 24: Secondary structure of the HCV 5'UTR



[illegible]

UPPER CASE = RIBO nucleotide
lower case = 2'-O-methyl nucleotide
u = 2'-deoxy-2'-amino Uridine
s = phosphorothioate
B = inverted deoxybasic moiety

**Figure 26A: Enzymatic nucleic acid mediated inhibition of
HCV-luciferase expression**

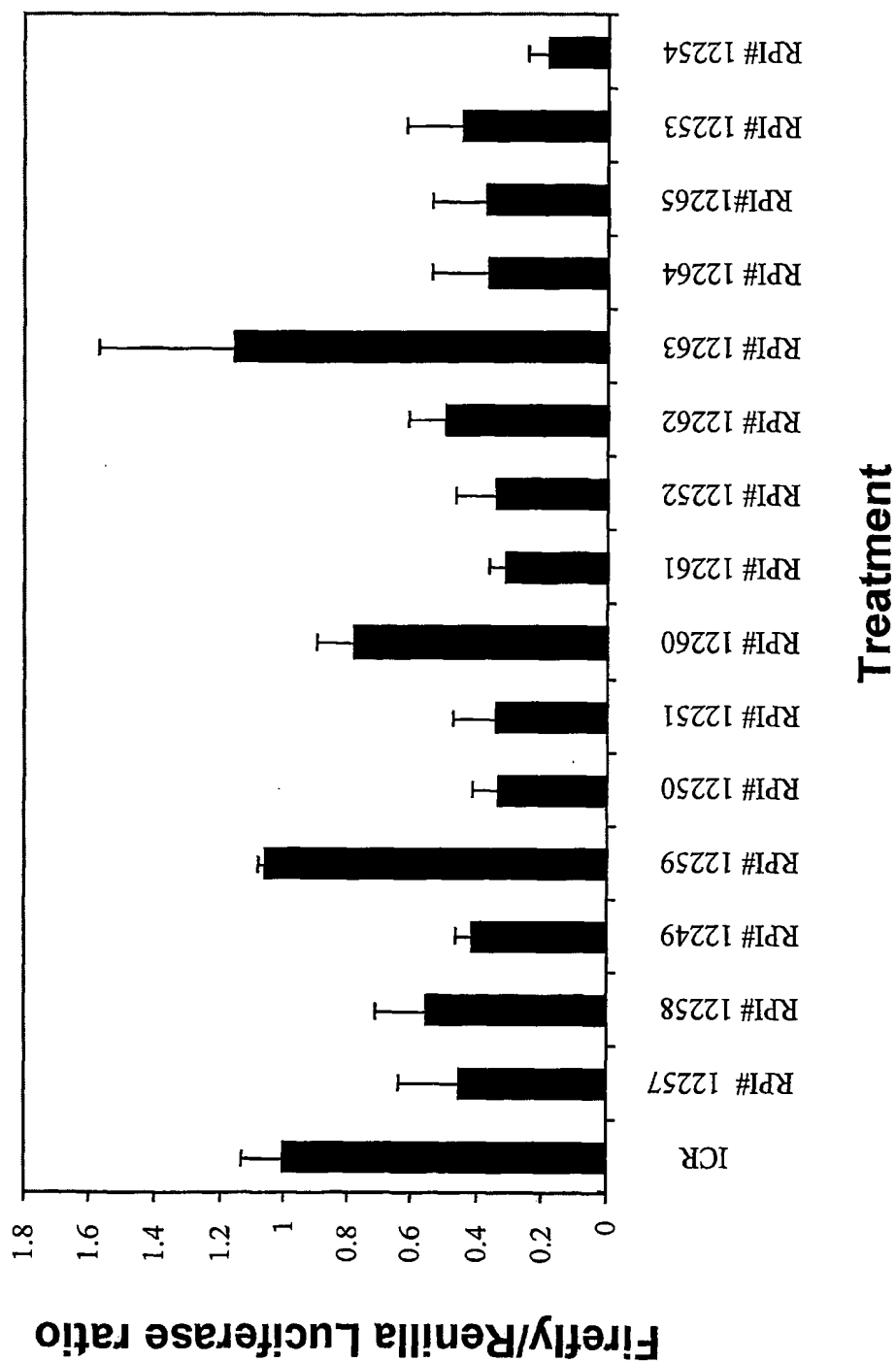
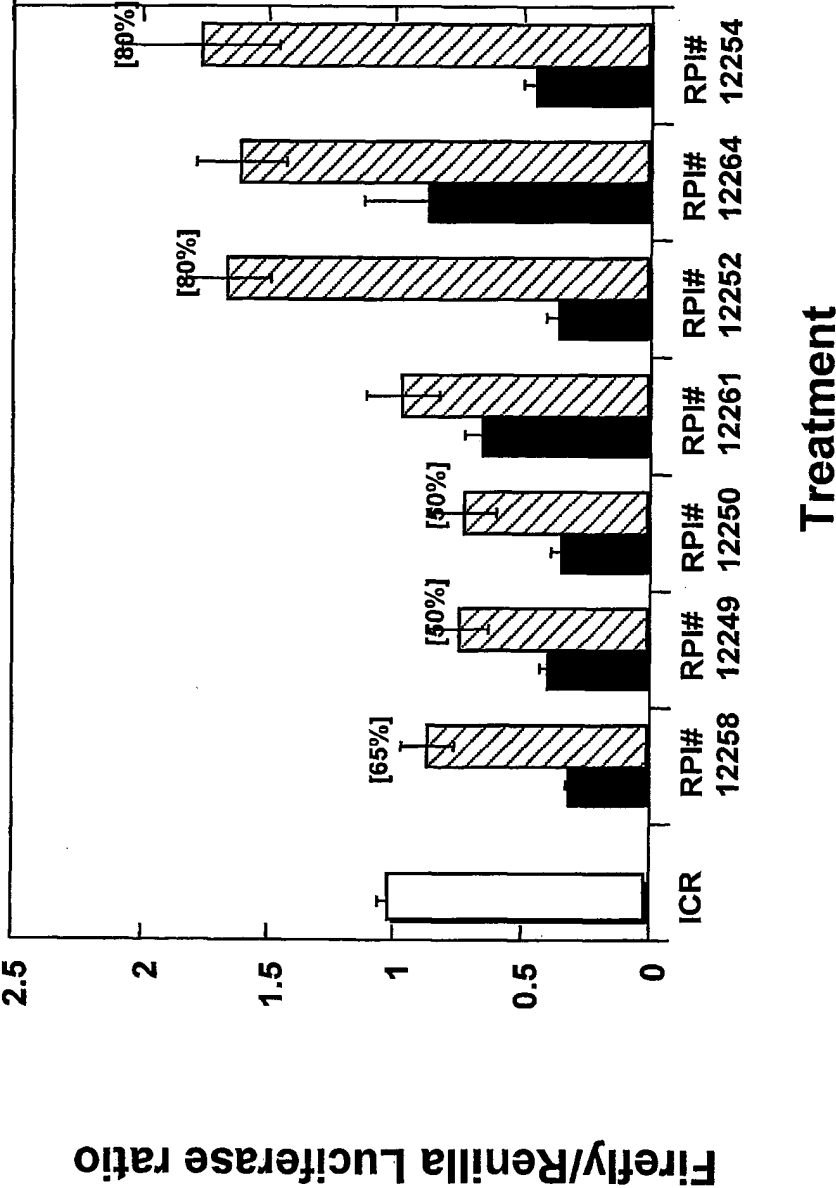


Figure 26B: Enzymatic nucleic acid mediated inhibition of HCV-luciferase expression



**Figure 27A: Dose-dependent enzymatic nucleic acid
inhibition of HCV/luciferase expression**

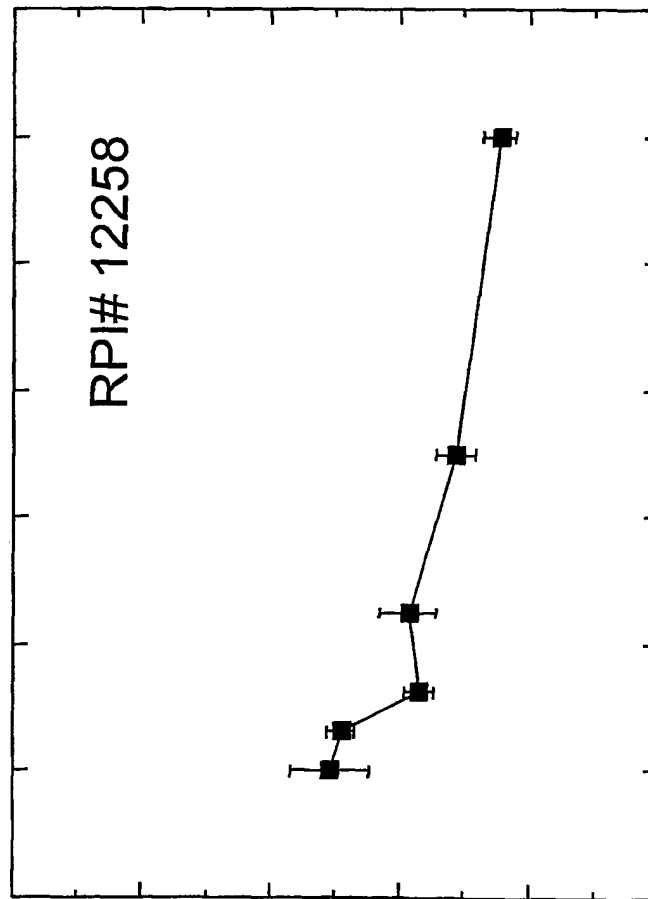


Figure 27B: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

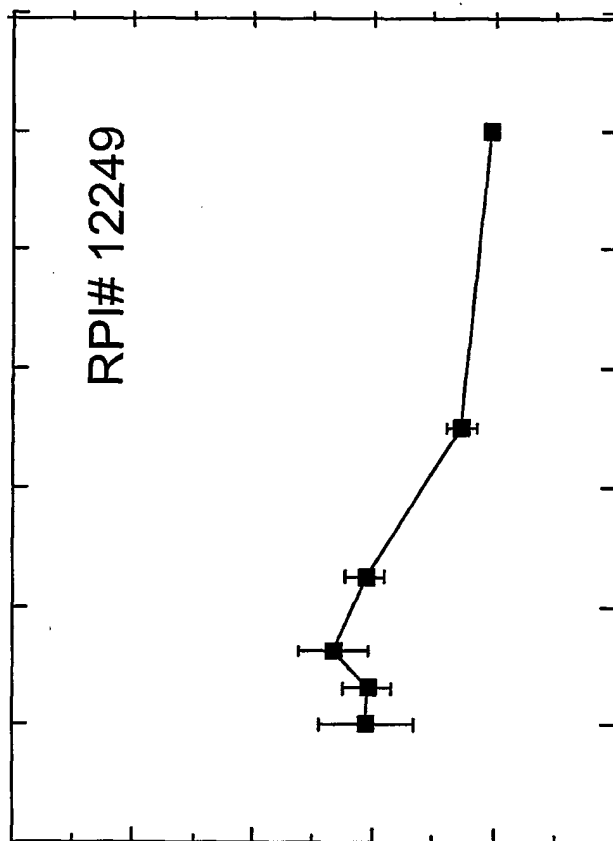


Figure 27C: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

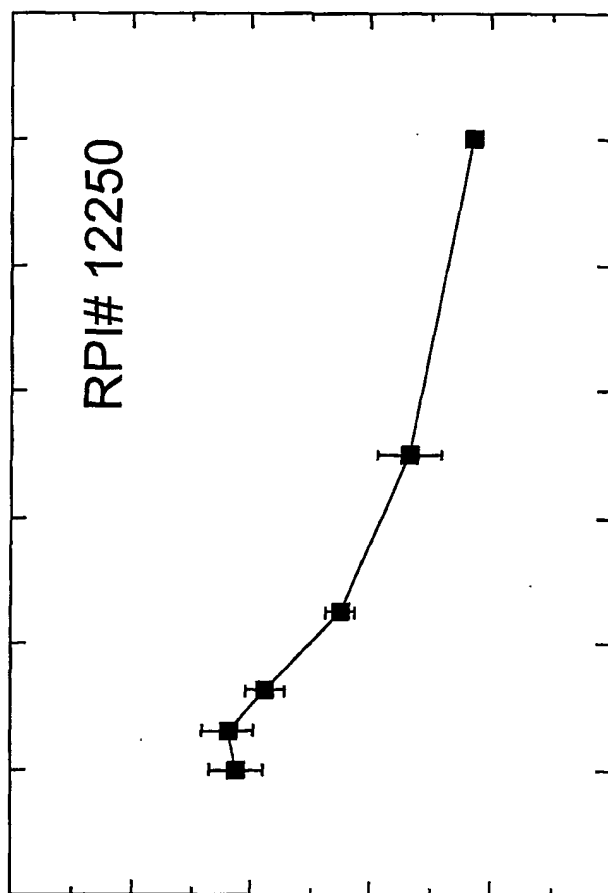


Figure 27D: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

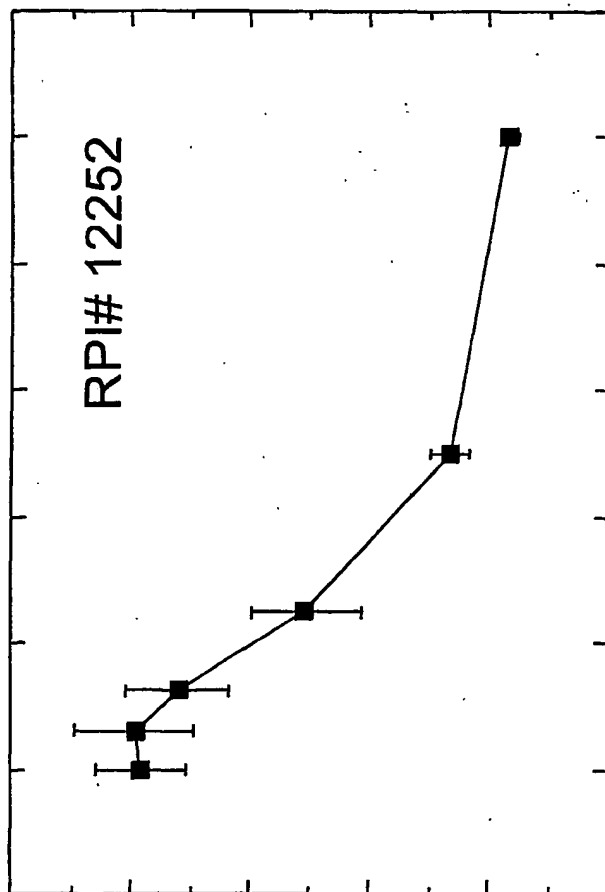


Figure 27E: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

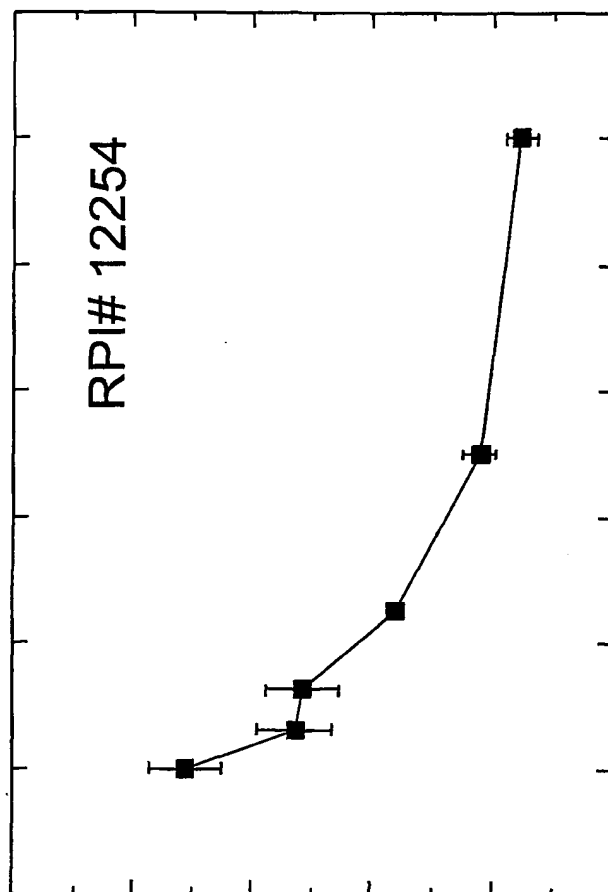


Figure 28A: Enzymatic nucleic acid reduction of HCV/luciferase RNA and inhibition of HCV-luciferase expression

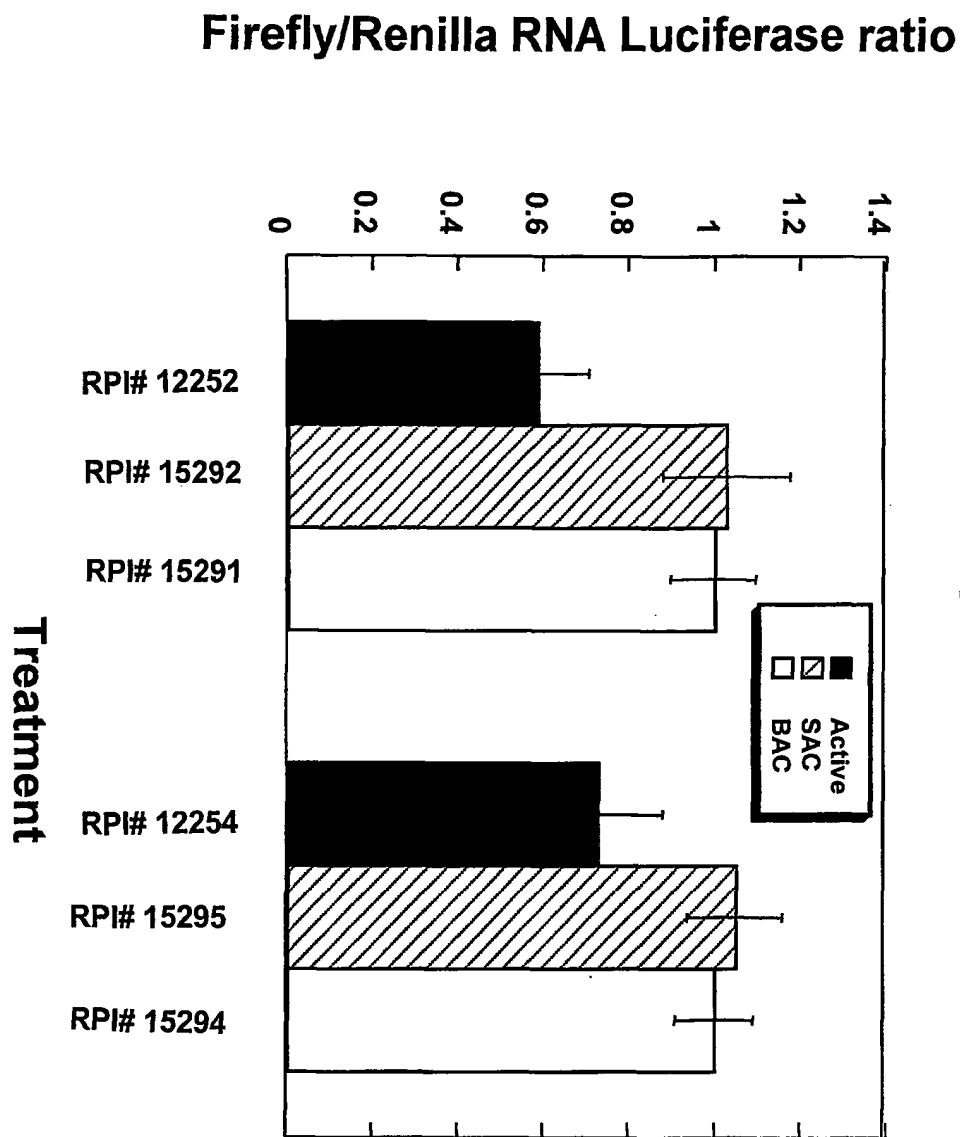
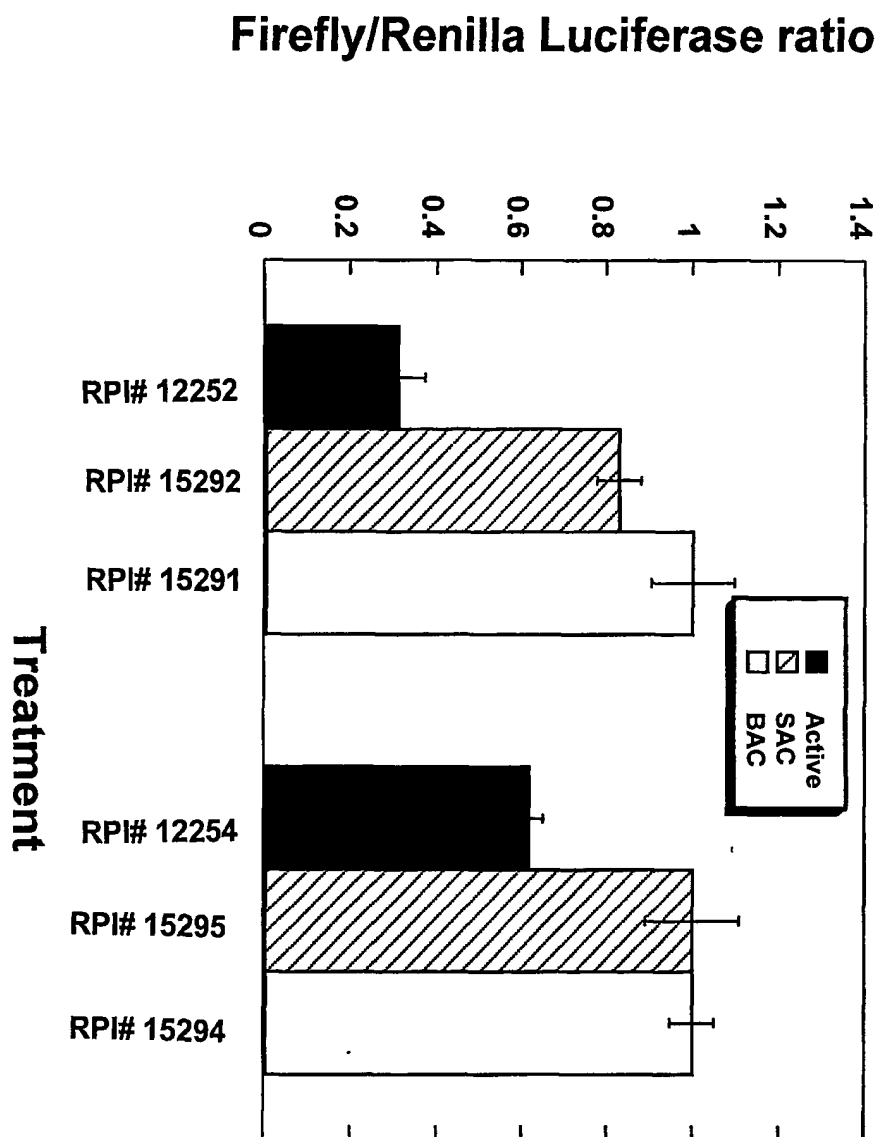
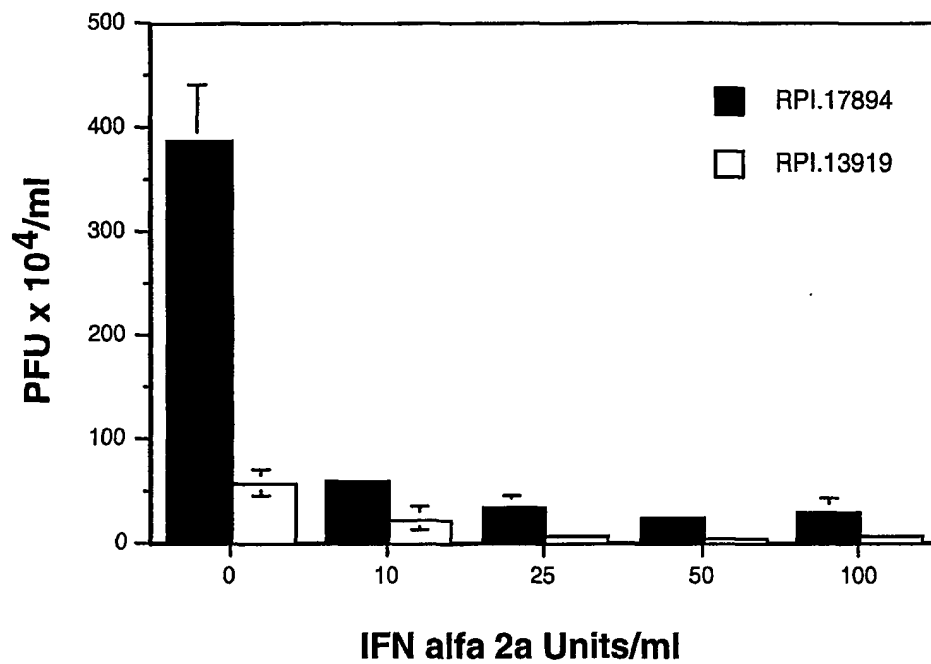


Figure 28B: Enzymatic nucleic acid reduction of HCV-luciferase RNA and inhibition of HCV-luciferase expression



***Figure 29A: Interferon Dose response with
Enzymatic Nucleic Acid***



***Figure 29B: Interferon Dose response with
Enzymatic Nucleic Acid***

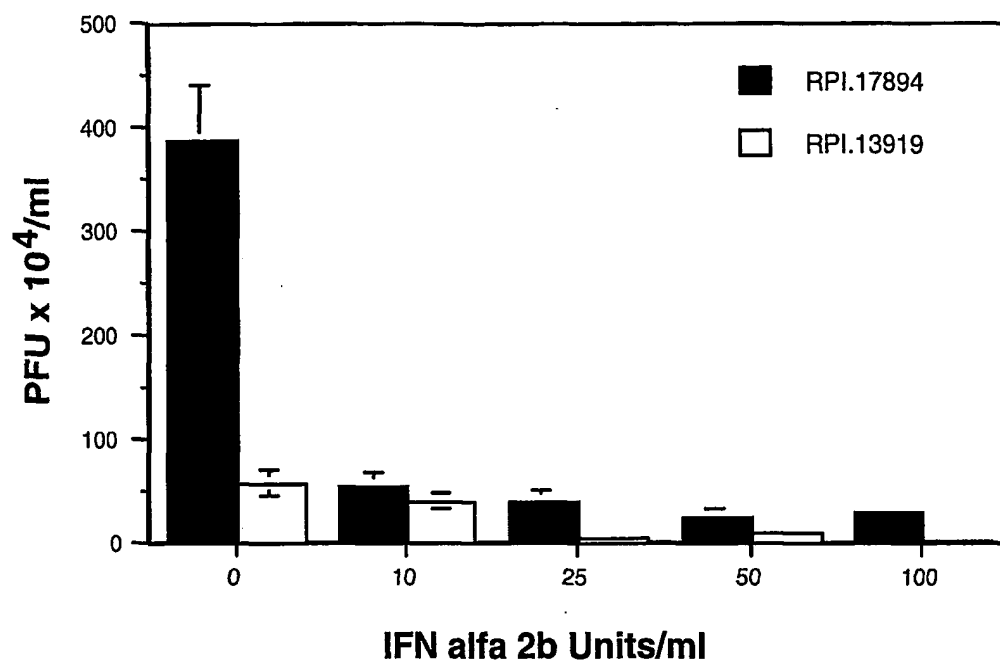
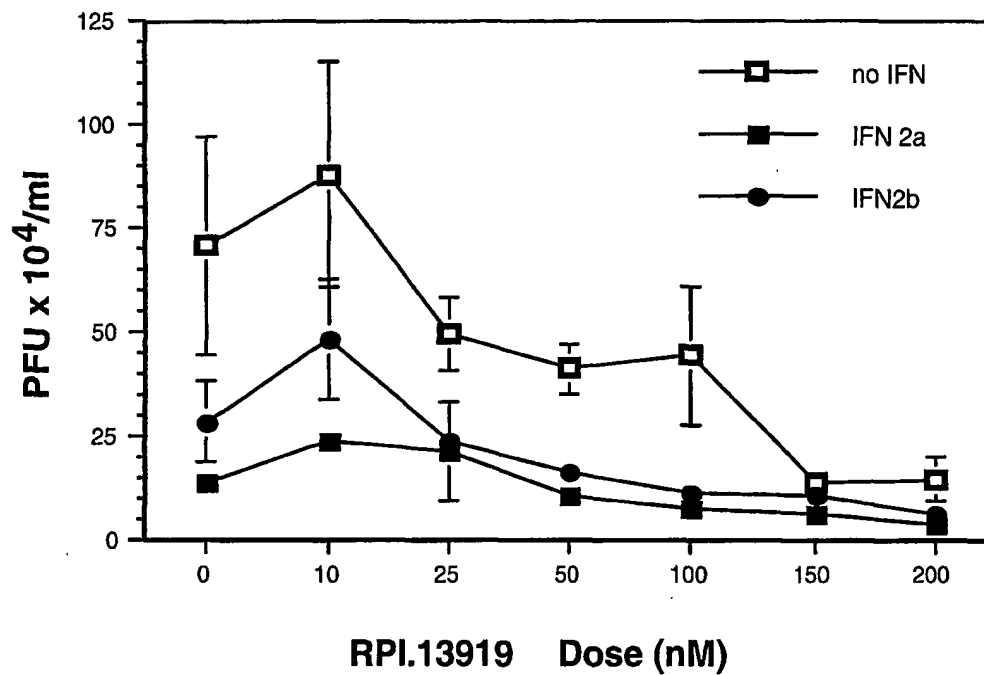


Figure 30: Site 195 anti-HCV enzymatic nucleic acid dose response in combination with interferon pretreatment



***Figure 31A: CIFN dose response with site 195
anti-HCV enzymatic nucleic acid treatment***

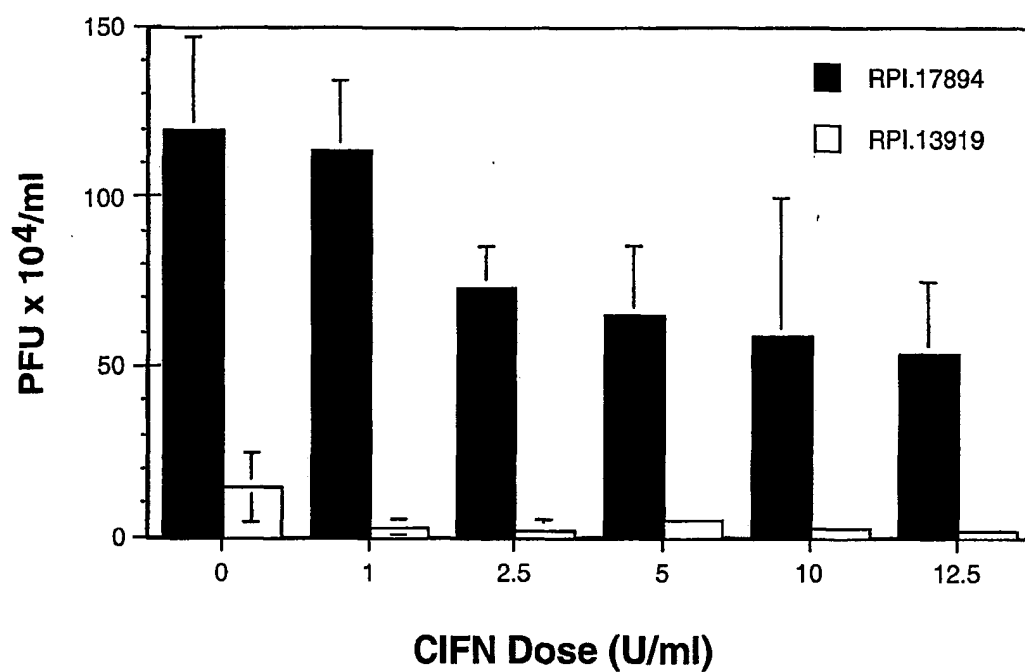


Figure 31B: Site 195 anti-HCV enzymatic nucleic acid dose response with CIFN pretreatment

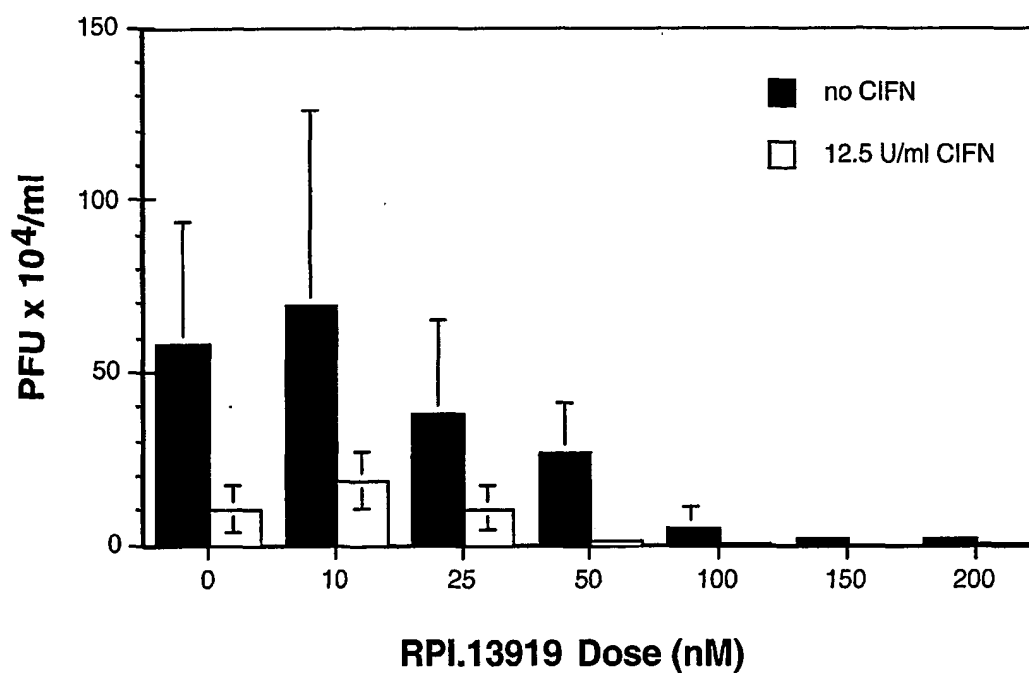
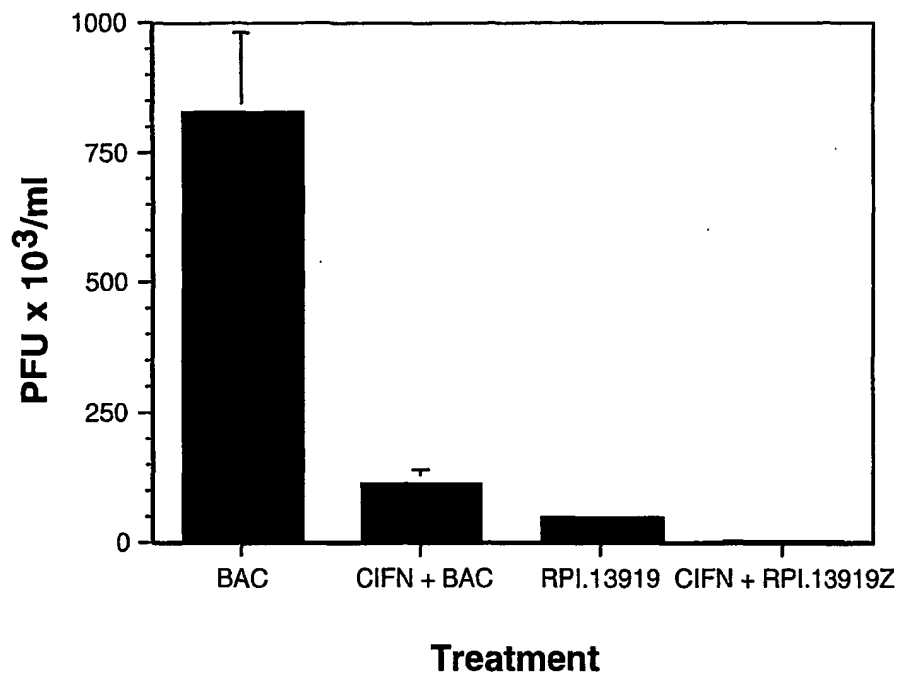


Figure 32: Enhanced antiviral effect of an anti-HCV enzymatic nucleic acid targeting site 195 used in combination with consensus interferon (CIFN)



**Figure 33: Inhibition of HCV-PV Replication
by Zinzyme Treatment**

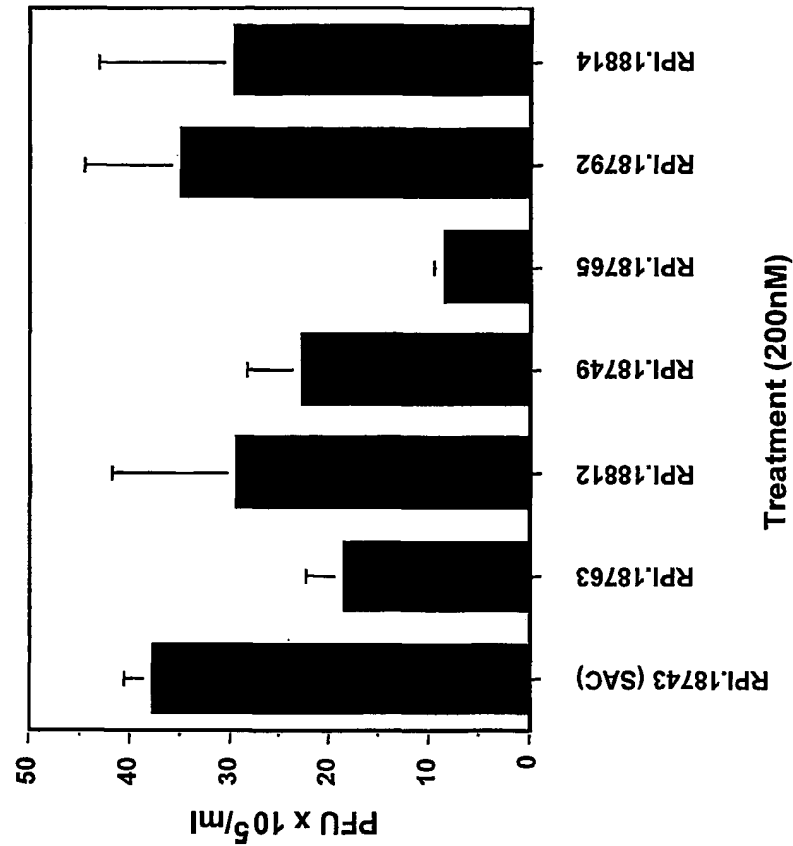


Figure 34: Inhibition of HCV-Poliovirus Replication by Antisense

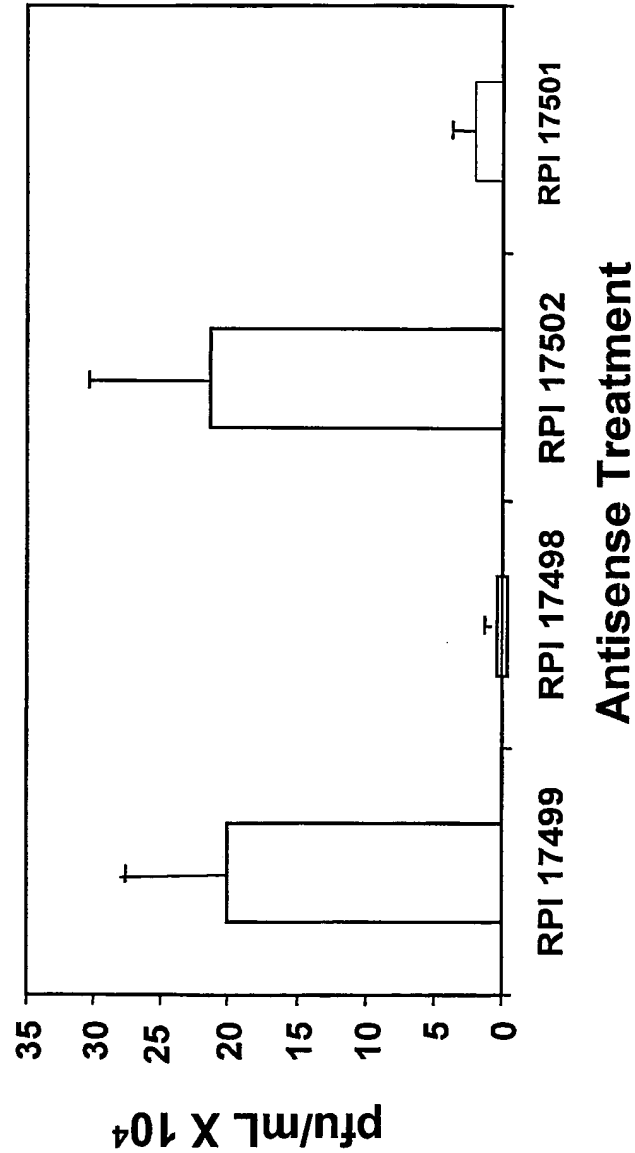


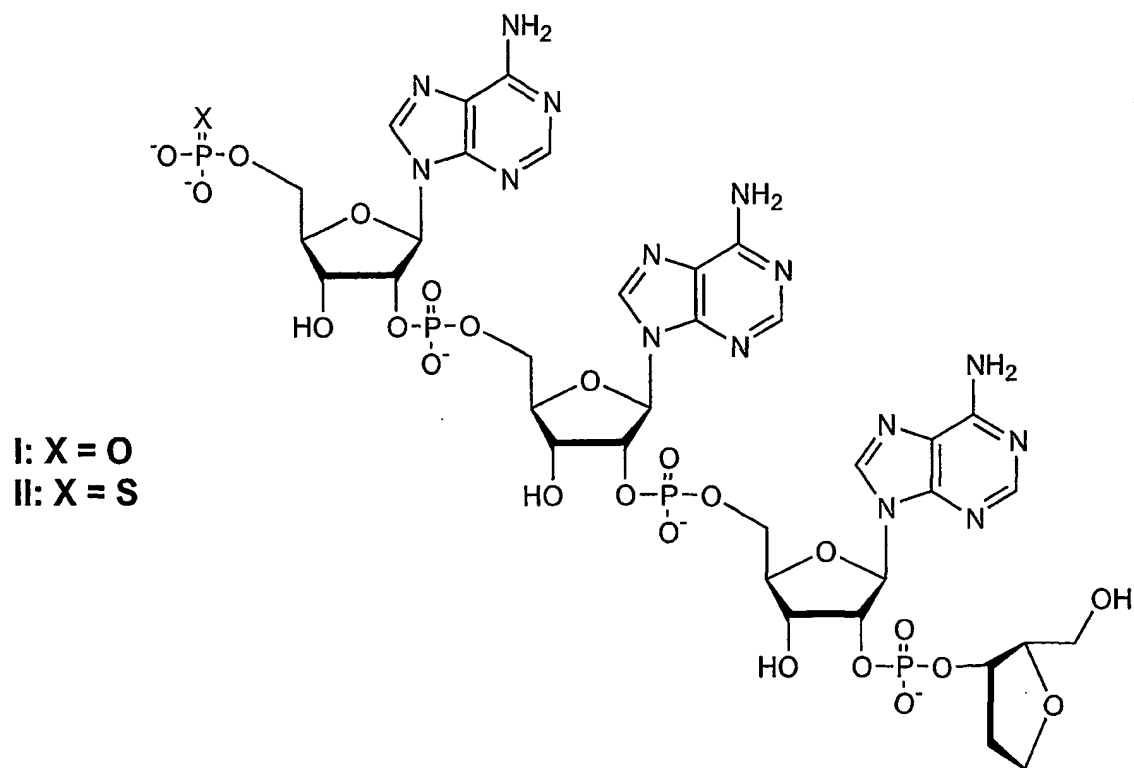
Figure 35: Modified 2-5A Compound

Figure 36A: Ribozyme activity and enhanced antiviral effect

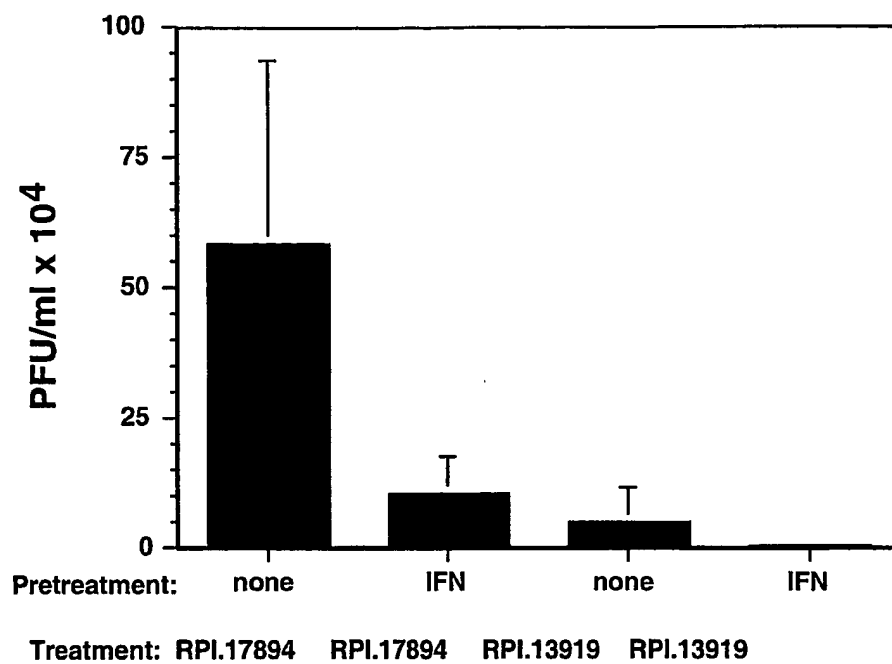


Figure 36B: Ribozyme activity and enhanced antiviral effect

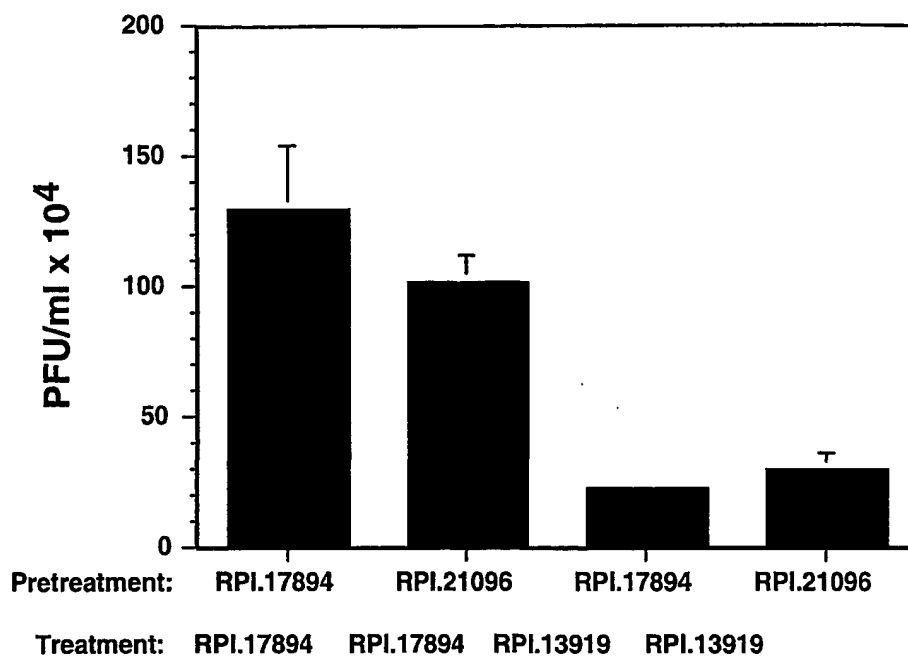


Figure 37: Inhibition of viral replication with anti-HCV ribozyme or 2-5A treatment

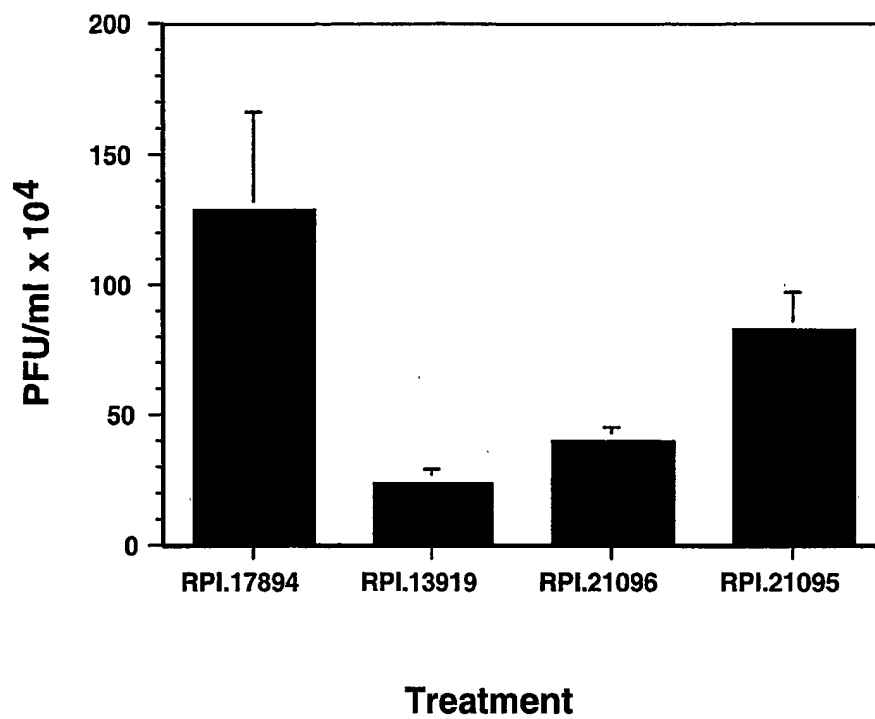


Figure 38: Anti-HCV ribozyme in combination with 2-5A treatment

